of the allene **13** in 10 mL of CH_2Cl_2, and the resulting solution was allowed to warm to room temperature. The reaction solution was concentrated under reduced pressure, mixed with 48.6 mg of (+)-borneol, and analyzed (HPLC). The products were the furan adducts **3** (5%), the dimer **4a** (5%), the dimer **4b** (20%), and the dimer **4c** (12%), accompanied by 6% of the bromo ketone **1b** and minor unidentified peaks at 7.7 and 26.4 min. In addition, three minor peaks were observed that corresponded in retention times to the dimers **14** of the allene **13**.

In a second experiment designed to test the possibility that the enone **2a** might react with the allene at 25 °C, a solution of 321 mg (1.40 mmol) bromo ketone **1b** in 2.56 g (21 mmol) of the allene **13** was mixed with 10 mL (13.7 g, 138 mmol) of Et_3N and heated to 35 °C with stirring. A white precipitate separated from the initially clear solution as the reaction proceeded. After the mixture had been heated with stirring for 36 h, it was poured into aqueous 1 M HCl and extracted with CH_2Cl_2. The organic extract was washed with aqueous NaCl, dried, and concentrated under reduced pressure. The residual yellow solid was mixed with 40.2 mg of (+)-borneol (an HPLC standard). The reaction mixture was subjected to preparative HPLC to separate 21 mg (7%) of the bromo ketone **1b**, 39.6 mg of borneol, 23.8 mg (12.5%) of dimer **4a**, and 154 mg (80.1%) of a mixture of dimers **4b** and **4c**. All products were identified with authentic samples by comparison of spectral data and/or by a mixture melting point determination.

Treatment of the Enone 2a with Molecular Oxygen. The cold (−78 °C) pyrolysate from 500 mg (2.45 mmol) of adduct **3** was dissolved in 25 mL of cold (−78 °C), anhydrous hexane and a stream of air (dried in a column packed with Drierite) was passed through the cold solution for 45 min. The resulting solution was allowed to warm to room temperature and then concentrated under reduced pressure and mixed with 45.5 mg of (+)-borneol for HPLC analysis. The crude product contained 2% of the furan adducts **3**, 2% of the dimer **4a**, 11% of the dimer **4b**, and 5% of the dimer **4c**. Additional small unidentified peaks were present at 7.8, 26.7, and 30.5 min.

Nucleophilic Addition of the Pentafluoroethyl Group to Aldehydes, Ketones, and Esters

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Pentafluoroethyl iodide reacts with methyllithium at −78 °C to produce (pentafluoroethyl)lithium. This halogen–metal exchange reaction can be carried out in the presence of aldehydes, ketones, and esters with no observable addition of methyllithium to the carbonyl derivative. The resultant (pentafluoroethyl)lithium adds to aldehydes and ketones in 80–100% yields to produce the corresponding secondary and tertiary carbinols. (Pentafluoroethyl)lithium adds to esters to give good yields of either ketones or tertiary carbinols. The nature of the product formed from the esters was a function of both the structure of the ester and the reaction conditions.

Recently, we communicated our results on the addition of (pentafluoroethyl)lithium to aldehydes and ketones.[1a] We now wish to provide the experimental details of this addition of (pentafluoroethyl)lithium[1b] to aldehydes and ketones and the extension of this nucleophilic addition to esters.

Introduction

The introduction of a small perfluoroalkyl group into an organic molecule is highly desirable in connection with both biological studies[2] and physical organic studies. In the former area, the highly lipophilizing nature of the perfluorinated alkyl group may favorably alter in vivo transport and absorption rates of a drug, while its inherent stability may improve the analogue's stability and in vivo half-life. In addition, the strong electron-withdrawing nature of the perfluoroalkyl group can greatly alter the chemistry of the molecule. These factors make the incorporation of a small perfluoroalkyl group a powerful tool in drug modification. The electronic properties of these substituents have also attracted physical organic chemists, who have used them in studies of destabilized carbocations[3] and reduced neighboring group participation by electron withdrawal.[4]

It was our interest in these latter areas which led us to look more closely at the methods currently available for the introduction of small perfluoroalkyl groups into organic molecules. In particular, we were interested in carbanionic-type additions to carbonyl containing functionalities. While the literature contains numerous reports of attempted introduction of a trifluoromethyl group using an organometallic reagent, there have been few successes.[5-7] Recent reports[8] utilizing transiently formed zinc reagents can be used with aldehydes, but the functionalization of ketones is much more problematic. (Trifluoromethyl)lithium[6] and Grignard[7] reagents are not synthetically useful as they decompose readily, apparently to difluorocarbene, even when formed at low temperature in the presence of a suitable electrophile. There is a marked increase in the stability of the organometallic with (heptafluoropropyl)lithium[9] and the heptafluoropropyl Grignard reagent.[10,11] While not entirely stable, these reagents

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(1) (a) For a preliminary report on this work, see: Gassman, P. G.; O'Reilly, N. J. *Tetrahedron Lett.* **1985**, *26*, 5243. Presented in part at the 191st National Meeting of the American Chemical Society, New York, NY, April 13–18, 1986; paper ORG 123. (b) For earlier reports on the use of (pentafluoroethyl)lithium see: Kawakami, K.; Kuivila, H. G. *J. Org. Chem.* **1969**, *34*, 1502. Solladiè-Cavallo, A.; Suffert, J. *Tetrahedron Lett.* **1984**, *25*, 1897. Solladiè-Cavallo, A.; Suffert, J. *Synthesis* **1985**, 659.

(2) See, for example: *Biomedical Aspects of Fluorine Chemistry*; Filler, R., Kobayashi, Y., Ed.; Kodansha and Elsevier: Amsterdam, 1983. Filler, R. *CHEMTECH* **1974**, 752. Smith, F. A. *CHEMTECH* **1973**, 422.

(3) Allen, A. D.; Kanagasapathy, V. M.; Tidwell, T. T. *J. Am. Chem. Soc.* **1986**, *108*, 3470 and references cited therein.

(4) Gassman, P. G.; Hall, J. B. *J. Am. Chem. Soc.* **1984**, *106*, 4267.

(5) Kitazume, T.; Ishikawa, N. *Nippon Kagaku Kaishi* **1984**, 1725.

(6) Pierce, O. R.; McBee, E. T.; Judd, G. F. *J. Am. Chem. Soc.* **1954**, *76*, 474.

(7) Haszeldine, R. N. *J. Chem. Soc.* **1954**, 1273.

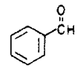
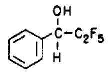
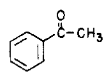
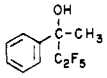
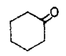
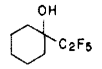
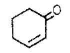
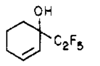
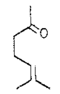
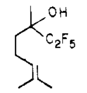
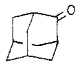
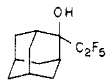
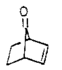
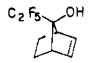
(8) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186; *Chem. Lett.* **1981**, 1679; **1982**, 137, 1453. O'Reilly, N. J.; Maruta, M.; Ishikawa, N. *Chem. Lett.* **1984**, 517.

(9) McBee, E. T.; Roberts, C. W.; Curtis, S. G. *J. Am. Chem. Soc.* **1955**, *77*, 6387. Beel, J. A.; Clark, H. C.; Whyman, D. *J. Chem. Soc.* **1962**, 4423.

(10) McBee, E. T.; Battershell, R. D.; Braendlin, H. P. *J. Org. Chem.* **1963**, *28*, 1131. Henne, A. L.; Francis, W. C. *J. Am. Chem. Soc.* **1951**, *73*, 3518.

0022-3263/87/1952-2481$01.50/0

Table I. Pentafluoroethylation of Aldehydes and Ketones with (Pentafluoroethyl)lithium

aldehyde or ketone	C_2F_5I, equiv	MeLi, equiv	time, min	product	% yield	bp, °C (mm)
	1.84	1.46	30		91	61-62 (2)[a]
	1.51	1.40	30		88	58-59 (3)
	1.77	1.77	8		100[b]	58-59 (11)
	1.56	1.24	30		81	59 (5)
	1.50	1.30	30		86	51 (1.5)
	1.61	1.44	30		93[b]	83-84 (2)
	1.19	1.17	45		84[b]	71-76 (12)

[a] Lit.[15] bp 214 °C (atmospheric). [b] Isolated by column chromatography.

and other lithium[12] and Grignard[13] reagents of higher members of the perfluoroalkyl homologous series have been used successfully at low temperatures. With this marked difference in chemistry between trifluoromethyl-substituted organometallics and heptafluoropropyl-substituted organometallics, it is remarkable that the chemistry of organometallics substituted by the second smallest perfluoroalkyl group, the pentafluoroethyl group, has not been the subject of detailed studies. Whereas the pentafluoroethyl Grignard reagent was first reported in 1957[11] it has been used only a few times since.[14,15] Recently, we have found that (pentafluoroethyl)lithium may be generated easily and efficiently by an exchange reaction between pentafluoroethyl iodide and methyllithium at −78 °C.[1] When the reagent is formed in the presence of an aldehyde or a ketone, the corresponding secondary or tertiary carbinols may be isolated in excellent yield. In the presence of an ester, the observed product was either the corresponding pentafluoroethyl-substituted ketone or the bis(pentafluoroethyl)-substituted carbinol. In many cases it was possible to selectively form either of these products by simple modifications of the experimental conditions.

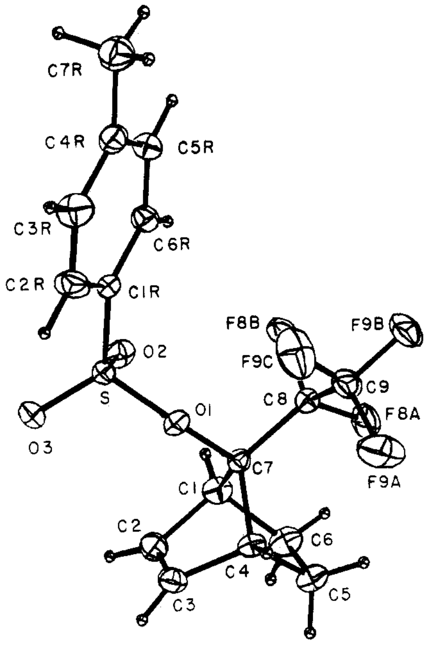


Figure 1. ORTEP drawing of 3.

Results and Discussion

Reaction of (Pentafluoroethyl)lithium with Aldehydes and Ketones. In a typical procedure, 1.2–1.8 equiv of a 1.6 M solution of methyllithium–lithium bromide in diethyl ether was added to an ethereal solution containing 1.0 equiv of a ketone or aldehyde and 1.2–1.8 equiv of pentafluoroethyl iodide, at −78 °C. As shown in Table I, the yields of purified (distilled or chromatographed) products were excellent, ranging from 81–100%. It was interesting to note that no products arising from attack of methyllithium on the starting carbonyl compound could be detected. This indicated that the exchange reaction between pentafluoroethyl iodide and methyllithium occurred at a rate which was much faster than the rate of addition of methyllithium to aldehydes and ketones.

With the first six carbonyl derivatives shown in Table I, the addition of (pentafluoroethyl)lithium was straightforward. However, the stereochemistry of addition of (pentafluoroethyl)lithium to the last compound on the list, bicyclo[2.2.1]hept-2-en-7-one (1) was difficult to assign. On the basis of preliminary ^1H and ^{13}C NMR spectral studies, we assigned a structure in which the hydroxyl group was anti to the double bond.[1a] In order to unequivocally establish the stereochemistry of this (pentafluoroethyl)lithium addition to 1, the resulting carbinol 2 was converted

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[11] McBee, E. T.; Roberts, C. W.; Meiners, A. F. *J. Am. Chem. Soc.* **1957**, *79*, 335.

[12] Adcock, J. L.; Renk, E. B. *J. Org. Chem.* **1979**, *44*, 3431. Denson, D. D.; Moore, G. J.; Sun, K. K.; Tamborski, C. *J. Fluorine Chem.* **1977**, *10*, 75. Johncock, P. *J. Organomet. Chem.* **1969**, *19*, 257.

[13] Denson, D. D.; Smith, C. F.; Tamborski, C. *J. Fluorine Chem.* **1973/1974**, *3*, 247. Smith, C. F.; Soloski, E. J.; Tamborski, C. *J. Fluorine Chem.* **1974**, *4*, 35.

[14] Thoai, N. *J. Fluorine Chem.* **1975**, *5*, 115. Von Werner, K.; Gisser, A. *J. Fluorine Chem.* **1977**, *10*, 387.

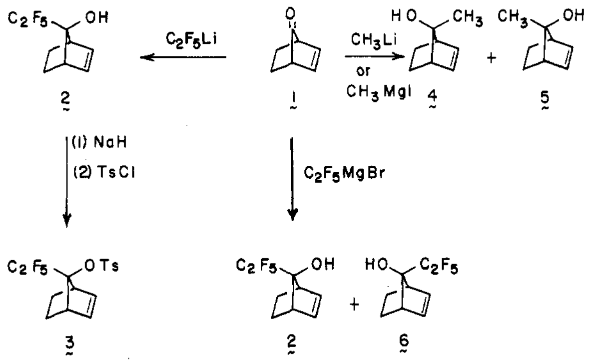
[15] Santini, G.; LeBlanc, M.; Reiss, J. G. *J. Organomet. Chem.* **1977**, *140*, 1.

Table II. Selected Bond Distances and Bond Angles for 7-*syn*-Hydroxy-7-*anti*-(pentafluoroethyl)-2-norbornenyl Tosylate (3)

atoms	angle, deg	atoms	angle, deg
O1–S–O2	110.11 (6)	C7–C8–C9	117.1 (1)
O1–S–O3	106.50 (6)	C7–C8–F8A	112.4 (1)
O1–S–C1R	100.16 (5)	C7–C8–F8B	109.5 (1)
O2–S–O3	119.26 (6)	C9–C8–F8A	105.2 (1)
O2–S–C1R	110.56 (6)	C9–C8–F8B	105.8 (1)
O3–S–C1R	108.49 (7)	F8A–C8–F8B	106.0 (1)
S–O1–C7	127.54 (7)	C8–C9–F9A	109.8 (1)
O1–C7–C1	117.7 (1)	C8–C9–F9B	109.7 (1)
O1–C7–C4	106.7 (1)	C8–C9–F9C	113.2 (1)
O1–C7–C8	102.7 (1)	F9A–C9–F9B	107.2 (1)
C1–C7–C4	93.88 (9)	F9A–C9–F9C	108.9 (1)
C1–C7–C8	116.9 (1)	F9B–C9–F9C	107.7 (1)
C4–C7–C8	119.3 (1)	S–C1R–C2R	119.6 (1)
C7–C1–C2	98.3 (1)	S–C1R–C6R	119.6 (1)
C7–C1–C6	102.3 (1)	C2R–C1R–C6R	120.8 (1)
C2–C1–C6	103.8 (1)	C1R–C2R–C3R	119.0 (1)
C1–C2–C3	107.9 (1)	C2R–C3R–C4R	121.4 (1)
C2–C3–C4	108.2 (1)	C3R–C4R–C5R	118.4 (1)
C7–C4–C3	98.34 (9)	C3R–C4R–C7R	121.0 (1)
C7–C4–C5	102.0 (1)	C5R–C4R–C7R	120.6 (1)
C3–C4–C5	105.1 (1)	C4R–C5R–C6R	121.1 (1)
C4–C5–C6	103.2 (1)	C1R–C6R–C5R	119.3 (1)
C1–C6–C5	103.3 (1)		
atoms	**distance, Å**	**atoms**	**distance, Å**
S–O1	1.596 (1)	C8–C9	1.540 (2)
S–O2	1.425 (1)	C8–F8A	1.346 (2)
S–O3	1.425 (A)	C8–F8B	1.357 (1)
S-C1R	1.751 (1)	C9–F9A	1.329 (2)
O1–C7	1.456 (2)	C9–F9B	1.332 (2)
C7–C1	1.553 (2)	C9–F9C	1.309 (2)
C7–C4	1.552 (2)	C1R–C2R	1.388 (2)
C7–C8	1.543 (2)	C1R–C6R	1.386 (2)
C1–C2	1.521 (2)	C2R–C3R	1.381 (2)
C1–C6	1.561 (2)	C3R–C4R	1.394 (2)
C2–C3	1.324 (2)	C4R–C5R	1.388 (2)
C3–C4	1.524 (2)	C4R–C7R	1.508 (2)
C4–C5	1.546 (2)	C5R–C6R	1.385 (2)
C5–C6	1.554 (2)		

to the corresponding crystalline *p*-toluenesulfonate derivative **3** and was subjected to single-crystal X-ray analysis. This X-ray study established that the hydroxyl group of the original adduct was syn to the double bond. Figure 1 provides an ORTEP drawing of **3** and Table II gives the structural parameters.

The reaction of methyllithium with **1** was first reported by Erman to give a 3:2 mixture of **4**/**5** at 0–5 °C.[16] Later,



Clark and Warkentin reported that this reaction at −75 °C gave a ratio of **4**/**5** varying from 2:1 to 4:1, depending on the solvent system employed.[17a] By comparison, the addition of methyl Grignard gave a 24:1 ratio of **4**/**5**.[17b] With this as background, the clean formation of **2** from **1** was surprising in that the stereochemistry of the addition reaction was dramatically altered (reversed). In view of this major change, we explored the addition of (pentafluoroethyl)magnesium bromide to **1** and found that a 24:1 mixture of **2**/**6** was formed in 74% yield. Thus, it would appear that the reversal of the direction of nucleophilic attack of the organometallic reagent on the carbonyl moiety of **1** is a function of the electronic character of the attacking anion.

Table III. Reaction of Cyclohexanone with Preformed Solutions of (Pentafluoroethyl)lithium[a] at -78 °C

C_2F_5Li, equiv[b]	period before addition	% yield[c]
1.2	30 min	96
1.2	8 h	64
1.2	19 h	42

[a] Reaction was carried out as in the standard procedure except that cyclohexanone was added after the period stated. [b] Based upon amount of methyllithium used. [c] Yields determined by GLC using decane as an internal standard (added after the workup).

In order to gain some insight into the lifetime of (pentafluoroethyl)lithium at −78 °C, we preformed the reagent through the addition of methyllithium to an ethereal solution of pentafluoroethyl iodide. The reagent was then stored at −78 °C for various periods of time before the addition of a known amount of cyclohexanone. The results of this investigation are summarized in Table III. These results indicate that the half-life of (pentafluoroethyl)lithium at −78 °C in ether solution is at least 8 h.

Reaction of (Pentafluoroethyl)lithium with Esters. Surprisingly little is known about the reaction of perfluoroalkyl organometallic reagents with esters. In the few studies which have been reported, the products have either been the corresponding ketones or the reduced secondary alcohols, depending on the conditions employed.[18-20] In the present study, (pentafluoroethyl)lithium was generated at −78 °C in the presence of a carboxylic ester. The results of these reactions, together with the experimental details, are summarized in Table IV.

In a typical procedure, 4.7–5.8 equiv of a 1.6 M solution of methyllithium–lithium bromide in diethyl ether was added to an ethereal solution containing 1.0 equiv of an ester and 4.9–7.4 equiv of pentafluoroethyl iodide, at −78 °C. After being stirred for 30 min at this temperature, the reaction was quenched with dilute mineral acid, and the product was extracted with ether. As can be seen from Table IV, the isolated yields of the products were good to excellent, and, in the majority of cases, a single product was formed. In no instance was the reduced secondary alcohol observed.

It is clear that the selectivity of the reaction was not dependent on the number of equivalents of reagent present. A comparison of experiments 1 and 2 shows that in each case an excess of (pentafluoroethyl)lithium was present; however, the type of products formed was com-

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(16) Erman, W. F. *J. Org. Chem.* **1967**, *32*, 765.

(17) (a) Clark, F. R. S.; Warkentin, J. *Can. J. Chem.* **1971**, *49*, 2223. (b) Warkentin, J. *Can. J. Chem.* **1970**, *48*, 1391.

(18) McBee and co-workers have studied the reaction of (heptafluoropropyl)lithium with ethyl heptafluorobutyrate: McBee, E. T.; Roberts, C. W.; Curtis, S. G. *J. Am. Chem. Soc.* **1955**, *77*, 6387.

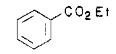
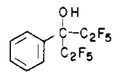
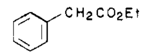
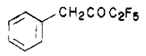
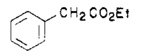
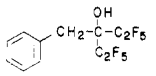
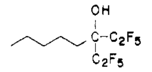
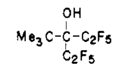
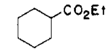
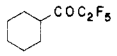
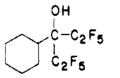
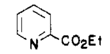
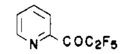
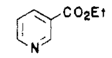
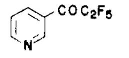
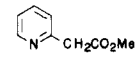
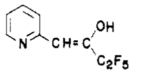
(19) The reactions of (heptafluoropropyl)magnesium iodide (a) with ethyl heptafluorobutyrate and ethyl formate and (b) with ethyl trifluoroacetate have been reported: (a) Henne, A. L.; Francis, W. C. *J. Am. Chem. Soc.* **1953**, *75*, 992. (b) Pierce, O. R.; Levine, M. *J. Am. Chem. Soc.* **1953**, *75*, 1254.

(20) Tamborski and co-workers have studied the reaction of longer-chain perfluoroalkyl Grignard and lithium reagents with diethyl carbonate and diethyl oxalate: Chen, L. S.; Chen, G. J.; Tamborski, C. *J. Fluorine Chem.* **1984**, *26*, 341.

(21) E. I. du Pont de Nemours and Co. (England, D.C.) Fr. Pat. 1325204, 1963; *Chem. Abstr.* **1963**, *59*, 11339g.

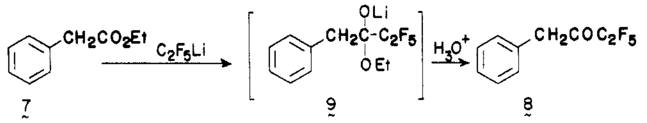
(22) McGrath, T. F.; Levine, R. *J. Am. Chem. Soc.* **1955**, *77*, 3656.

Table IV. Reaction of (Pentafluoroethyl)lithium with Esters at -78 °C

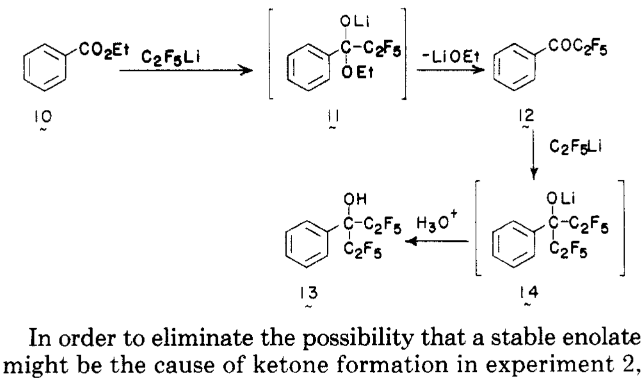
expt	ester	C_2F_5I, equiv	MeLi, equiv	product	% yield	bp, °C (mm)
1		5.0	5.0		62[a]	55-56 (4)[b]
2		5.3	5.1		74	65-66 (7)
3[c]		7.1	5.0		90	51-53 (1)
4		6.1	5.8		66	50-51 (8)
5	Me_3CCO_2Et	5.8	5.0	 $\mathrm{Me_3C{-}C(OH)(C_2F_5){-}C_2F_5}$	93[d]	70-73 (40)
6		6.2	5.0		39	66-73 (32)
					24	93-95 (32)
7	$MeSCH_2CO_2Et$	6.1	5.0	$MeSCH_2COC_2F_5$	62[e]	111-112 (atmos), 63-64 (84)
8		4.9	4.7		71[f,g]	56-57 (4)
9		6.5	5.0		78[f,g]	58-60 (7)
10		7.4	5.1		100[f,h]	[mp 96-97[i]]

[a] Passed through a silica column with hexane prior to distillation. [b] Lit.[21] bp 81 °C (3mm). [c] After the mixture was stirred for 30 min at - 78 °C, the cooling bath was removed, and stirring was continued for 1 h. [d] Solvent was removed by distillation through a 13-cm Vigreaux column. [e] Distilled from phosphorus pentoxide. [f] After the usual extraction, the aqueous layer was rendered basic (red litmus test) with potassium carbonate and further extracted with diethyl ether. [g] These compounds readily form hydrates upon standing. [h] Based on ester consumed (82% recovery). Product was isolated by preparative-scale MPLC (10% ethyl acetate in hexane on silica) and recrystallized from hexane. [i] Lit.[22] mp 98-98.8 °C (reported as ketone).

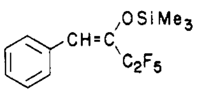
pletely different. The selectivity of the reaction appears to be due to the relative stabilities of the intermediate lithiated hemiketals as illustrated by the conversion of **7** into **8** via the intermediacy of **9**.



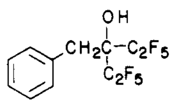
These results indicate **9** is stable at -78 °C, while **11**, formed from ethyl benzoate (**10**), is not. The differing stability of these lithiated hemiketals would depend in each case on a balance between steric destabilization and electronic stabilization. In the case of the ethyl benzoate adduct **11**, decomposition occurs to give the corresponding pentafluoroethyl-substituted ketone **12**, which may then react further with the excess (pentafluoroethyl)lithium present in solution to give the observed product **13** via **14**.



In order to eliminate the possibility that a stable enolate might be the cause of ketone formation in experiment 2, we attempted to trap the intermediate as the trimethylsilyl enol ether **15**. Repeating experiment 2 and following its progress by GLC showed that an 81% yield of the ketone, together with 14% yield of the corresponding tertiary carbinol, was obtained when a sample from the reaction mixture was quenched after 30 min at -78 °C. If a large excess of trimethylsilyl chloride was added at this point and the reaction mixture was allowed to warm to room temperature and stirred for 10 h before an acid workup, the trimethylsilyl enol ether **15** was observed in 81% yield, together with only a 15% yield of **8** and 2.5% of the tertiary carbinol **16**. Thus, an enolate was formed under these reaction conditions. However, when the reaction mixture was maintained at -78 °C for 8 h after adding the trimethylsilyl chloride and then allowed to warm to room temperature and stirred for a further 13 h, a 43% yield of **8**, a 16% yield of **16**, and a 41% yield of **15** was observed. A sample taken from this reaction mixture and quenched with acid just before the mixture was warmed to room temperature showed an 83% yield of **8**, a 15% yield of **16**, and a 1% yield of **15**. These results strongly suggest that an intermediate was present at -78 °C which does not react with either (pentafluoroethyl)lithium or with trimethylsilyl chloride and which decomposes upon warming above -78 °C. Furthermore, quenching this intermediate with acid affords the ketone. The lithiated hemiketal **9** is an intermediate which would be consistent with the observed

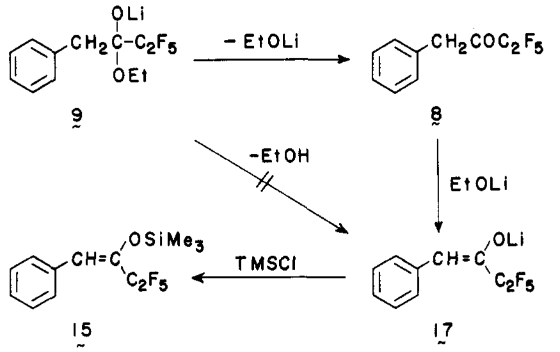


15



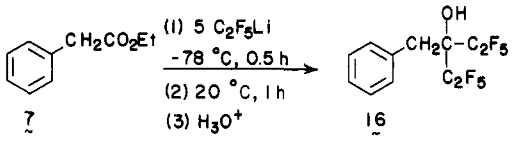
16

Scheme I



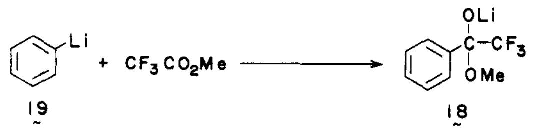
results. Additional studies showed that treatment of the pentafluoroethyl-substituted ketone **8** with (pentafluoroethyl)lithium at −78 °C resulted in an 80% yield of **16**, with 5% of **8** remaining. If the enolate **17** was not formed by proton abstraction from the ketone by (pentafluoroethyl)lithium, the only alternative is abstraction by lithium ethoxide which was formed upon decomposition of **9**. Experimentally, treatment of **8** with lithium ethoxide in ether followed by an excess of trimethylsilyl chloride led to an 88% yield of the trimethylsilyl ether **15** (50% conversion). Scheme I below illustrates the processes which seem likely to be occurring. It would seem that the direct conversion of **9** into **17** via loss of ethanol was not occurring to a significant extent.

These results suggest that an alteration of the reaction conditions would lead to high yields of the carbinol. Thus, in experiment 3, the carbinol **16** was isolated in high yield when the reaction mixture was allowed to warm to room temperature after an initial period at −78 °C.

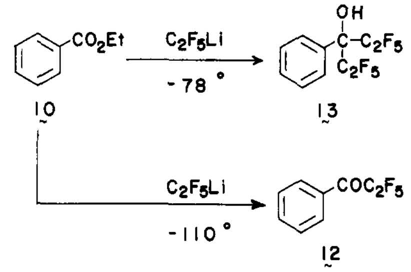


The stability of the intermediate hemiketal salts would seem to be the reason for ketone formation in several other experiments (see Table IV, experiments 6–10). In the pyridyl cases the intermediate may be stabilized by nitrogen coordination with lithium, and it is possible that a similar stabilization occurs with sulfur in entry 7. However, it is not clear why the corresponding hemiketal salt in entry 6 should be more stable than those derived from the *n*-pentyl- and *tert*-butyl-substituted ethyl carboxylates in entries 4 and 5, respectively, though it is possible that steric congestion may be responsible.

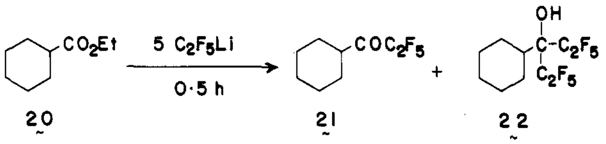
There is good precedent for the intermediacy of lithiated hemiketals in this type of reaction. McBee and co-workers proposed such an intermediate in the reaction of (heptafluoropropyl)lithium with ethyl heptafluorobutyrate,[18] and Chen et al. have isolated and characterized the salt **18** from the reaction of phenyllithium (**19**) with methyl trifluoroacetate.[23]

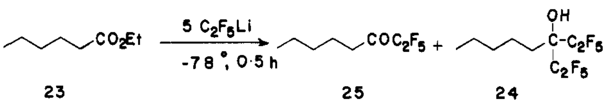


The sensitivity of the intermediate hemiketal salts to temperature can be employed advantageously. In experiment 1 of Table IV, the carbinol **13** was the only isolated product. Reducing the reaction temperature to −110 °C improved the stability of the intermediate lithiated hemiketal and allowed us to isolate the corresponding ketone **12** in 74% yield. It seemed likely that the low yield of **13** in experiment 1 was due to the formation of some ketone and that this might be minimized by allowing the reaction mixture to warm to room temperature before quenching, thereby allowing the intermediate to decompose fully to the ketone which could then react further to give the carbinol. Repeating experiment 1 using the experimental modification employed in experiment 3 resulted in the observation of the carbinol **13** as the sole product, which was isolated in 78% yield.



The effects of temperature and of localized heating and cooling efficiency on this reaction cannot be overemphasized. As shown in entry 6 of Table IV, the reaction of ethyl cyclohexanecarboxylate (**20**) with an excess of (pentafluoroethyl)lithium under the standard conditions (in a 100-mL flask at the maximum possible concentration of (pentafluoroethyl)lithium of ca. 0.6 M) afforded a mixture of **21** and **22**. When the reaction was run on a smaller scale with a 25-mL flask (more efficient heat transfer) and more dilute conditions (0.31 M), we observed a 97% yield of **21** with only 3% of **22** (GLC yields). Similarly when the reaction temperature was reduced to −110 °C (using a 100-mL flask at 0.42 M (pentafluoroethyl)lithium concentration), we observed exclusive formation of **21** (100% yield, 40% conversion after 0.5 h by GLC analysis). These results are important in that they indicate the sensitivity of the reactions to changes in bath temperature and other factors affecting the dissipation of heat from the reaction mixture. Results consistent with those found for **20** have been found for ethyl hexanoate (**23**). Under standard conditions (100-mL flask, 0.60 M (pentafluoroethyl)lithium) the corresponding carbinol **24** was isolated in 66% yield (Table IV, entry 4). In order to test the reproducibility of this result, the reaction was repeated under essentially the same reaction conditions (100-mL flask, 0.58 M (pentafluoroethyl)lithium) and **24** was isolated in 67% yield. However, running the reaction on a smaller scale (50-mL flask) and use of more dilute conditions (0.33 M (pentafluoroethyl)lithium), we observed an 85% yield of the ketone **25** and only 2% of **24** (GLC yields). By retaining the 50-mL flask but increasing the concentration (0.68 M (pentafluoroethyl)lithium) a reduced amount of **25** (62%) and an increased amount of **24** (38%) was obtained (GLC yields).





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[23] Chen, L. S.; Chen, G. J.; Tamborski, C. *J. Fluorine Chem.* **1981**, *18*, 117.

These results indicated the borderline thermal stability of the intermediate lithiated hemiketals in these reactions. Thus, it is recommended that, if the ketone is the desired product, the reaction temperature and concentration of reactants be kept as low as possible. When carrying out the reaction on a large scale it would be advisable to add the methyllithium slowly (our attempts at precooling the methyllithium proved experimentally difficult). Should the desired product be the carbinol, the yield may be optimized by allowing the reaction mixture to warm to room temperature with stirring for 1 h before workup.

Experimental Section[24]

General Procedure for Reaction of Aldehydes and Ketones with (Pentafluoroethyl)lithium. Under anhydrous conditions and a dry nitrogen atmosphere, a 100-mL, three-necked flask cooled in a dry ice/isopropyl alcohol bath was charged with anhydrous diethyl ether (30 mL), acetophenone (1 mL, 1.03 g, 8.57 mmol), and pentafluoroethyl iodide (3.18 g, 12.93 mmol). The mixture was magnetically stirred, and a methyllithium/lithium bromide solution (1.6 M in diethyl ether, 7.5 mL, 12.0 mmol) was added. Stirring was continued for 30 min at −78 °C, after which time the flask contents were added to a 3 N aqueous hydrochloric acid solution (75 mL) together with 25 mL of diethyl ether. After being shaken, the layers were separated, and the aqueous layer was extracted with an additional 25 mL of diethyl ether. The combined ethereal extracts were dried over anhydrous sodium sulfate and filtered, and the solvent was removed with a rotary evaporator. Distillation of the residue gave 3-hydroxy-1,1,1,2,2-pentafluoro-3-phenylbutane (1.81 g, 88%): bp 58–59 °C (3 mm).

In all cases, preparative-scale GLC (10% OV101, 10 ft × 0.25 in., 125–185 °C) afforded an analytical sample. This general procedure was used for a series of aldehydes and ketones with the minor modification outlined as follows: In the case of experiments 3, 6, and 7 (Table I), after the solvent was removed, the product was purified by chromatography on a silica column eluting with a hexane/methylene chloride solvent gradient.

Spectral data for the compounds prepared by this general procedure are listed below.

1-(Pentafluoroethyl)cyclohexanol: ^{1}H NMR ($CDCl_3$) δ 1.78 (s, 1 H exchangeable with deuterium oxide) and 1.68 (s, 10 H); ^{13}C NMR ($CDCl_3$) δ 119.60 (q of t, J_{CF} = 288.0 Hz, J_{CCF}= 36.9 Hz), 114.90 (t of q, J_{CF} = 259.6 Hz, J_{CCF} = 34.8 Hz), 73.58 (t, J_{CCF} = 22.7 Hz), 29.64 (t), 24.88 (t), and 20.12 (t); IR (solid melt) 3405 s (broad O–H stretch), 2930 s, 2860 m, 1448 m, 1390 w, 1368 m, 1344 m, 1332 s, 1330 w, 1289 s, 1270 s, 1210 vs, 1180 vs, 1152 s, 1127 vs, 1088 s, 1058 s, 1052 m, 1039 m, 988 vs, 970 m, 925 vw, 907 m, 890 m, 870 m, 840 w, 824 m, 737 s, and 679 s cm^{-1}; exact mass M_r calcd for $C_8H_{11}F_5O$ m/e ($M - H_2O$) 200.0624, found 200.0619.

Anal. Calcd for $C_8H_{11}F_5O$: C, 44.04; H, 5.08. Found: C, 44.09; H, 5.09.

3-Hydroxy-3-(pentafluoroethyl)cyclohexene: ^{1}H NMR ($CDCl_3$) δ 6.16 (d of d of d, J = 10.2, 4.9, and 2.6 Hz, 1 H), 5.77 (d, J = 10.2 Hz, 1 H), 2.45 (s, 1 H, exchangeable with deuterium oxide), and 2.17–1.77 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 136.19 (d), 122.92 (d), 119.55 (q of t, J_{CF} = 287.6 Hz, J_{CCF} = 36.6 Hz), 114.83 (t of q, J_{CF} = 259.4 Hz, J_{CCF} = 34.9 Hz), 71.43 (t, J_{CCF} = 23.1 Hz), 29.14 (t), 24.79 (t), and 17.25 (t); IR (neat) 3610 w, 3400 m (broad O–H stretch), 3040 w, 2940 m, 2870 w, 2835 w, 1667 w, 1446 m, 1432 7, 1403 m, 1375 w (broad), 1338 s, 1270 w, 1220–1165 vs, 1140 vs, 1110 m, 1090 s, 1080 s, 1065 s, 1052 s, 1025 w, 994 s, 970 s, 939 s, 905 m, 892 s, 850 m, 740 s, 730 s, and 718 m cm^{-1}; exact mass M_r calcd for $C_8H_9F_5O$ m/e 216.0573, found 216.0577.

Anal. Calcd for $C_8H_9F_5O$: C, 44.45; H, 4.20. Found: C, 44.64; H, 4.31.

1-Hydroxy-1-phenyl-2,2,3,3,3-pentafluoropropane:[15] ^{1}H NMR ($CDCl_3$) δ 7.50–7.45 (m, 5 H), 5.08 (d of d of d, J_{HF} = 16.6 and 7.7 Hz, J = 5.1 Hz, 1 H), and 3.16 (d, J = 5.1 Hz, 1 H, exchangeable with deuterium oxide) [lit.[15] (CCl_4) δ 4.9, (d of d, J = 14 Hz, J = 10 Hz)]; ^{13}C NMR ($CDCl_3$) δ 133.85 (s), 129.74 (d), 128.66 (d), 127.89 (d), 119.11 (q of t, J_{CF} = 286.7 Hz, J_{CCF} = 35.7 Hz), 113.07 (d of d of q, J_{CF} = 255.1 and 260.6 Hz, J_{CCF} = 35.7 Hz), and 72.00 (d of d, J_{CCF} = 27.7 and 22.4 Hz); IR (neat) 3440–3390 m (broad O–H stretch), 3090 vw, 3068 w, 3038 w, 2980 w, 2940–2875 w (broad), 1500 m, 1460 m, 1390 w, 1370 m, 1340 m, 1331 m, 1215–1202 s, 1190–1177 s, 1132–1122 m, 1095 m, 1062 m, 1031 s, 1010 m, 1000 w, 920 vw, 850 w, 830 m, 820 w, 754 m, 731 m, 716 s, 695 s, 640 w, and 622 m cm^{-1}.

3-Hydroxy-1,1,1,2,2-pentafluoro-3-phenylbutane: ^{1}H NMR ($CDCl_3$) δ 7.15–7.10 (m, 5 H), 2.51 (s, 1 H, exchangeable with deuterium oxide), and 1.77 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.55 (s), 128.54 (d), 128.24 (d), 126.10 (d), 119.31 (q of t, J_{CF} = 287.9 Hz, J_{CCF} = 36.5 Hz), 114.39 (t of q, J_{CF} = 261.5 Hz, J_{CCF} = 34.6 Hz), 75.12 (t, J_{CCF} = 24.0 Hz) and 24.60 (q); IR (neat) 3480 m (broad O–H stretch), 3095 vw, 3060 w, 3030, w, 3000 w, 2940 vw, 1610 w, 1500 w, 1475 w, 1465 w, 1452 m, 1385 w, 1340 m, 1285 w, 1273 w, 1220–1210 vs, 1203–1180 vs, 1134 s, 1108 s, 1076 m, 1063 m, 1030 w, 1007 s, 928 w, 915 w, 818 w, 759 m, 742 m, 735 m, 696 s, and 663 w cm^{-1}; exact mass M_r calcd for $C_{10}H_9F_5O$ m/e 240.0573, found 240.0572.

Anal. Calcd for $C_{10}H_9F_5O$: C, 50.01; H, 3.78. Found: C, 50.23; H, 3.93.

7-*syn*-Hydroxy-7-*anti*-(pentafluoroethyl)bicyclo[2.2.1]hept-2-ene (2): ^{1}H NMR ($CDCl_3$) δ 6.25 (s, 2 H), 3.03 (s, 2 H), 2.78 (s, 1 H, exchangeable with deuterium oxide), 2.07–2.02 (m, 2 H), and 1.09–1.04 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 134.25 (d), 119.42 (q of t, J_{CF} = 287.5 Hz, J_{CCF} = 36.6 Hz), 115.40 (t of q, J_{CF} = 259.8 Hz, J_{CCF} = 36.4 Hz), 89.78 (t, J_{CCF} = 24.4 Hz), 48.15 (d), and 22.13 (t); IR (neat) 3580 m, 3500–3465 m (broad O–H stretch), 3065 w, 2990 m, 2965 m, 2930 w, 2895 m, 1645 vw, 1475 w, 1459 w, 1443 w, 1428 vw, 1372 m, 1340 s, 1317 s, 1303 m, 1225–1215 vs, 1192 vs, 1180 vs, 1140 vs, 1101 s, 1081 s, 1053 vs, 1021 s, 1010 w, 995 vw, 971 w, 955 w, 928 w, 899 s, 882 w, 862 m, 836 s, 820 w, 803 w, 780 w, 764 vw, 734 vs, 721 s, 710 m, 695 w, and 650 w cm^{-1}; exact mass M_r calcd for $C_9H_9F_5O$ m/e 228.0573, found 228.0575.

Anal. Calcd for $C_9H_9F_5O$: C, 47.37; H, 3.98. Found: C, 47.28; H, 4.08.

2-Hydroxy-2-(pentafluoroethyl)adamantane: ^{1}H NMR ($CDCl_3$) δ 2.27–2.12 (m, 6 H), 1.93 (s, 1 H, exchangeable with deuterium oxide), 1.90–1.79 (m, 2 H), 1.75 (s, 4 H), 1.63 (s, 1 H), and 1.59 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 119.63 (q of t, J_{CF} = 289.0 Hz, J_{CCF} = 37.1 Hz), 116.82 (t of q, J_{CF} = 263.4 Hz, J_{CCF} = 33.9 Hz), 76.04 (t, J_{CCF} = 21.9 Hz), 38.28 (t), 33.46 (t), 33.21 (t of t, J_{CCCF} = 4 Hz), 32.85 (d), 26.75 (d), and 26.10 (d); IR (neat) 3605 m, 3490 m, 2925 vs, 2905 vs, 2870 s, 1482 m, 1466 s, 1450 m, 1360 m, 1335 s, 1330 s, 1308 m, 1284 w, 1253 m, 1218–1168 vs, 1130 vs, 1116 s, 1102 vs, 1093 vs, 1082 vs, 1062 m, 1096 s, 1089 s, 1017 s, 992 s, 959 s, 935 s, 900 s, 882 m, 842 m, 830 m, 800 w, 770 vw, 737 s, 682 m, 654 w, and 633 w cm^{-1}; exact mass M_r calcd for $C_{12}H_{15}F_5O$ m/e 270.1043, found 270.1058.

Anal. Calcd for $C_{12}H_{15}F_5O$: C, 53.33; H, 5.60. Found: C, 53.38; H, 5.64.

3,7-Dimethyl-3-hydroxy-1,1,1,2,2-pentafluoro-6-octene: ^{1}H NMR ($CDCl_3$) δ 5.12 (t of q, J = 5.9 and 1.4 Hz, 1 H), 2.20–2.09 (m, 2 H), 2.09 (s, 1 H, exchangeable with deuterium oxide), 1.77–1.66 (m, 2 H), 1.70 (s, 3 H), 1.63 (s, 3 H), and 1.40 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 133.07 (s), 123.08 (d), 119.45 (q of t, J_{CF} = 287.8 Hz, J_{CCF} = 36.7 Hz), 115.11 (t of q, J_{CF} = 259.8 Hz, J_{CCF} = 34.8 Hz), 74.50 (t, J_{CCF} = 22.6 Hz), 35.07 (t), 25.71 (q), 21.33 (t), 20.31 (q), and 17.65 (q); IR (neat) 3615 w, 3480–3440 m (broad O–H stretch), 2970 m, 2920 m, 2900–2860 m, 1670 vw, 1475 m, 1465 m, 1455 m, 1385 m, 1340 m, 1210–1198 s, 1190 s, 1120–1110 s, 1035 m, 1020 m, 1000 s, 970 m, 880 w, 860 w, 825 m, 750 m, and 672 m cm^{-1}; exact mass M_r calcd for $C_{10}H_{15}F_5O$ m/e 246.1043, found 246.1036.

Anal. Calcd for $C_{10}H_{15}F_5O$: C, 48.78; H, 6.14. Found: C, 48.95; H, 6.22.

7-*syn*-Hydroxy-7-*anti*-(pentafluoroethyl)-2-norbornenyl Tosylate (3). A 100-mL, round-bottomed, three-necked flask

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(24) Elemental analyses were performed by the Scandanavian Microanalytical Laboratory, Herlev, Denmark. Melting and boiling points are uncorrected. Proton magnetic resonance spectra were recorded on Varian CFT-20, Bruker AC-300, Bruker AC-200, and Nicolet NIC 1180E nuclear magnetic resonance spectrometers. Carbon magnetic resonance spectra were recorded on Bruker AC-300, Varian CFT-20, and Nicolet NIC 1180E spectrometers. Infrared spectra were recorded on a Beckman Model 4240 infrared spectrometer either neat on sodium chloride plates (for oils and liquids) or as potassium bromide pellets (for solids). Mass spectra were recorded on an AEI MS30 spectrometer.

was charged with 0.48 g (2.1 mmol) 7-*syn*-hydroxy-7-*anti*-(pentafluoroethyl)-2-norbornene, 20 mL of anhydrous diethyl ether, and 0.13 g (5.4 mmol) of sodium hydride under a dry nitrogen atmosphere. The reaction mixture was stirred for 3.5 h at room temperature, and 1.14 g (5.98 mmol) of freshly purified *p*-toluenesulfonyl chloride was then added. Stirring was continued for 45 h, and the reaction mixture was then poured into a separatory funnel containing 50 mL of water and 50 mL of hexane. After shaking and separating the layers, the aqueous layer was extracted with two additional 25-mL portions of hexane. The combined extracts were dried over anhydrous sodium sulfate and filtered, and the solvent was removed on a rotary evaporator. The resulting oil was chromatographed on a silica gel column with 250 mL of hexane as eluent. This afforded 0.65 g (57% recovery) of pure tosyl chloride, mp 66–67 °C. Further elution with 100 mL of ethyl acetate gave 0.71 g of an oil, which was shown by GLC (OV101 capillary) to consist of a mixture of product and starting material. Recrystallization from 10 mL of pentane at −78 °C gave 0.35 g (0.92 mmol, 44%) of **3** as a white solid, mp 76.5–79.0 °C. Repeated recrystallization from pentane at low temperature afforded X-ray quality crystals: mp 80.5–81.0 °C; ^{1}H NMR ($CDCl_3$) δ 7.70 and 7.28 (A_2X_2 system, J = 8.4 Hz, 2 H, 2 H), 6.05 (s, 2 H), 3.49 (s, 2 H), 2.43 (s, 3 H), 2.01 (s, 1 H), 1.98 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 144.31 (s), 135.44 (s), 133.12 (d), 129.28 (d), 127.65 (d), 118.93 (q of t, J_{CF} = 288.9 Hz, J_{CCF} = 36.94 Hz), 113.27 (t of q, J_{CF} = 263.3 Hz, J_{CCF} = 37.1 Hz), 102.24 (t, J_{CCF} = 24.9 Hz), 47.35 (d), 21.88 (t of t, J_{CCCCF} = 4.3 Hz), 21.65 (q); IR (KBr) 3095 vw, 3085 vw, 3070 vw, 3040 w, 3020 w, 3005 m, 2990 w, 2980 w, 2940 w, 2930 w, 2910 w, 1630 w, 1605 m, 1504 m, 1500 w, 1480 m, 1468 m, 1455 w, 1445 w, 1405 w, 1370 vs, 1349 w, 1320 s, 1308 w, 1296 w, 1241 m, 1225 vs, 1210 vs, 1196–1180 vs, 1162 s, 1150 vs, 1137 s, 1121 s, 1100 m, 1073 s, 1035 w, 1012 vs, 976 s, 962 s, 945 w, 916 s, 910 s, 875 m, 840 vs, 833 vs, 814 m, 800 m, 790 s, 740 s, 715 s, 705 m, 669 vs, 647 m, 610 s, 590 w, 570 s, 540 s cm^{-1}; exact mass M_r calcd for $C_{16}H_{15}F_5O_3S$ *m/e* 382.0662, found 382.0650.

Anal. Calcd for $C_{16}H_{15}F_5O_3S$: C, 50.26; H, 3.95. Found: C, 50.45; H, 4.03.

The white crystals of $C_{16}H_{15}F_5O_3S$ belonged to the centrosymmetric space group $P2_1/a$. The measured cell constant, a = 14.221 (4) Å, b = 8.118 (4) Å, c = 14.494 (3) Å, β = 109.44 (2)°, gave a calculated density of 1.653 g/cm^3 for the four molecules in the unit cell at −95 (2) °C. Data were collected on a fully automated Enraf-Nonius CAD4 diffractometer by using a variable rate W–2θ scan technique and graphite monochromatized Mo Kα radiation (λ = 0.71069 Å). After Lorentz polarization corrections, 2544 of 3147 unique reflections (81%) with $2\theta \leq 56$ were observed for $[F_o > \sigma(F_o)^2]$. A combination of direct methods and difference Fourier synthesis was used to locate all non-hydrogen atoms.[25] The non-hydrogen atoms were refined by full-matrix least-squares analysis with anisotropic thermal parameters; the hydrogen atoms were included at calculated positions with fixed B = 3. The R factor for the structure was 0.044.

Reaction of Bicyclo[2.2.1]hept-2-en-7-one (1) with (Pentafluoroethyl)magnesium Bromide. A 50-mL, round-bottomed, three-necked flask was charged with 0.13 g (1.2 mmol) of bicyclo[2.2.1]hept-2-en-7-one, 15 mL of anhydrous diethyl ether, and 0.72 g (2.9 mmol) of pentafluoroethyl iodide at −78 °C under a dry nitrogen atmosphere. To the stirred reaction mixture was added 0.7 mL (2.1 mmol) of a 3.0 M solution of ethylmagnesium bromide in diethyl ether. A sticky precipitate rapidly formed, and this halted the stirring. After 20 min the reaction mixture was allowed to warm to room temperature and stirred for an additional 2 h. The reaction mixture was then poured into a seperatory funnel containing 50 mL of 1 N hydrochloric acid solution and 20 mL of diethyl ether. After the layers were shaken and separated, the aqueous layer was extracted with an additional 30 mL of diethyl ether. The combined ethereal extracts were dried over anhydrous sodium sulfate and filtered, and 0.35 g of dodecane (as internal GLC standard) was added. GLC analysis (OV101 capillary) indicated the presence of 190 mg (71%) of *syn*-7-hydroxy-*anti*-7-(pentafluoroethyl)bicyclo[2.2.1]hept-2-ene (**2**) and 8 mg (3%) of *anti*-7-hydroxy-*syn*-7-(pentafluoroethyl)bicyclo[2.2.1]hept-2-ene (**6**).

Carbinol **6** exhibited the following physical characteristics: bp 54–56 °C (5 mm); ^{1}H NMR ($CDCl_3$) δ 5.95 (t, $^5J_{HF}$ = 2.1 Hz, 2 H), 2.84 (s, 2 H), 2.19 (s, 1 H, exchangeable with deuterium oxide), 2.02 (d, J = ca. 8.4 Hz, 2 H), 1.07 (d, J = ca. 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 132.06 (d), 119.33 (q of t, J_{CF} = 287.3 Hz, J_{CCF} = 36.6 Hz), 115.44 (t of q, J_{CF} = 260.3 Hz, J_{CCF} = 36.1 Hz), 90.34 (t, J_{CCF} = 18.1 Hz), 46.27 (d), and 23.14 (t); IR (neat) 3620 m, 3500–3440 m (broad), 3070 w, 2980 m, 2950 m, 2875 w, 1712 w (broad), 1462 w, 1450 w, 1344 s, 1302 w, 1285 m, 1216 s, 1205 s, 1185 s, 1162 m, 1145 m, 1128 s, 1100 m, 1089 m, 1083 m, 1048 m, 1030 m, 980 m, 929 w, 905 m, 880 w, 862 w, 849 m, 794 w, 786 w, 740 m, 712 s cm^{-1}; exact mass M_r calcd for $C_9H_9F_5O$ *m/e* 228.0573, found 228.0569.

Anal. Calcd for $C_9H_9F_5O$: C, 47.37; H, 3.98. Found: C, 47.57; H, 3.92.

General Procedure for the Reaction of (Pentafluoroethyl)lithium with Esters. A typical procedure is described for the reaction of ethyl phenylacetate with (pentafluoroethyl)lithium. A 100-mL, round-bottomed, three-necked flask was charged with 0.82 g (5.0 mmol) of ethyl phenylacetate, 30 mL of anhydrous diethyl ether, and 6.47 g (26.3 mmol) of pentafluoroethyl iodide at −78 °C under a dry nitrogen atmosphere. To the stirred solution was added 16 mL (25.6 mmol) of a 1.6 M solution of methyllithium/lithium bromide complex in diethyl ether. The reaction mixture was stirred for 0.5 h and then poured into a separatory funnel containing 80 mL of a 1 N aqueous hydrochloric acid solution and 50 mL of diethyl ether. After the layers were shaken and separated, the aqueous layer was further extracted with 25 mL of diethyl ether, and the combined extracts were dried over anhydrous sodium sulfate. After filtration and the solvent was removed on a rotary evaporator and the product was distilled under reduced pressure to give 0.88 g (3.7 mmol, 74%) of 1,1,1,2,2-pentafluoro-4-phenylbutan-3-one: bp 65–66 °C (7 mm); ^{1}H NMR ($CDCl_3$) δ 7.39–7.31 (m, 3 H), 7.23–7.16 (m, 2 H), and 4.04 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 191.72 (t, J_{CCF} = 26.7 Hz), 130.18 (s), 129.65 (d), 128.88 (d), 127.90 (d), 117.78 (q of t, J_{CF} = 286.8 Hz, J_{CCF} = 34.1 Hz), 107.23 (t of q, J_{CF} = 267.4 Hz, J_{CCF} = 38.3 Hz), and 43.84 (t); IR (neat) 3095 vw, 3075 w, 3040 w, 3010 vw, 2900 vw, 1765 s, 1705 m, 1608 w, 1590 w, 1502 m, 1460 w, 1433 w, 1405 w, 1362 m, 1338 m, 1320 w, 1215 s, 1195 s, 1185 m, 1165 m, 1136 w, 1112 w, 1085 w, 1070 m, 1032 w, 1005 w, 985 w, 972 w, 958 m, 945–920 w, 885 vw, 827 vw, 782 w, 745 m, 712 s, and 690 m cm^{-1}; exact mass M_r calcd for $C_{10}H_7F_5O$ *m/e* 238.0417, found 238.0426.

Anal. Calcd for $C_{10}H_7F_5O$: C, 50.43; H, 2.96. Found: C, 50.57; H, 3.02.

In the case of all liquids, analytical samples were prepared by preparative-scale GLC (10% OV101, 10 ft × 0.25 in., 60–180 °C).

This general procedure was used for a series of esters with the minor modifications outlined below:

(a) In experiment 1 (Table IV), the crude product was passed through a short silica column (eluted with hexane) prior to distillation.

(b) In experiment 3 (Table IV), after the reaction mixture was stirred for 30 min at −78 °C, the cooling bath was removed, and stirring was continued for 1 h before the usual workup and isolation.

(c) The product from experiment 5 (Table IV) was quite volatile. Therefore, after the usual workup, the solvent was removed by distillation through a 13-cm Vigreaux column. The product was then purified by distillation.

(d) The product from experiment 7 (Table IV) was found to form a hydrate readily, after initial distillation, and was therefore redistilled from phosphorus pentoxide and protected from moisture.

(e) In experiments 8–10 (Table IV), after the usual extraction, the aqueous layer was rendered basic (tested with red litmus) with potassium carbonate and was further extracted with two 50-mL portions of diethyl ether. These extracts were combined with the initial extracts and the total was dried over anhydrous sodium sulfate and the product was isolated in the usual manner.

(f) The products from experiments 8 and 9 (Table IV) readily form hydrates and had to be protected from moisture.

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[25] All calculations were carried out on a PDP 11/34 computer by using the Enraf-Nonius SDP programs. This crystallographic computing package is described by: Frentz, B. A. In *Computing in Crystallography*; Schench, M., Oltof-Hazekamp, R., van Konigweld, M., Bassie, G. S., Eds.; Delft University: Delft, Holland, 1978; pp 64–71.

(g) In experiment 10 (Table IV), after the modified workup described in e above, the solvent was removed on a rotary evaporator, and the product and recovered starting material were isolated by MPLC on a silica column eluting with 10% ethyl acetate in hexane. The product was further purified by recrystallization from hexane.

Spectral data for the products are given below.

1,1,1,2,2,4,4,5,5,5-Decafluoro-3-hydroxy-3-phenylpentane:[21] ^{1}H NMR ($CDCl_3$) δ 7.73 (d, 2 H, J = 7 Hz), 7.45 (m, 3 H), and 3.68 (s, 1 H, exchangeable with deuterium oxide); ^{13}C NMR ($CDCl_3$) δ 130.36 (d), 128.42 (d), 128.14 (s), 127.19 (d), 118.44 (q of pentets, J_{CF} = 289.1 Hz), 114.06 (t of q, J_{CF} = 274.7 Hz, J_{CCF} = 35.3 Hz), and 76.23 (pentet, J_{CCF} = 21.3 Hz); IR (neat) 3620 s, 3570 m, 3080 w, 3060–3040 w, 1610 w, 1500 m, 1460 m, 1365 m, 1340 m, 1315 s, 1245–1220 vs, 1200–1180 vs, 1155 vs, 1130 w, 1088 s, 1040–1030 w, 1004 w, 915 s, 895 m, 842 w, 822 s, 760 m, 720 s, 706 vs, and 623 m cm^{-1}; exact mass M_r calcd for $C_{11}H_6F_{10}O$ *m/e* 344.0259, found 344.0237.

3-Hydroxy-1,1,1,2,2-pentafluoro-3-(pentafluoroethyl)octane: ^{1}H NMR ($CDCl_3$) δ 2.92 (s, 1 H, exchangeable with deuterium oxide), 2.03 (t, J = 8 Hz, 2 H), 1.54 (pentet, J = 8 Hz, 2 H), 1.33 (m, 4 H), and 0.91 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 118.76 (q of t, J_{CF} = 288.0 Hz, J_{CCF} = 35.5 Hz), 113.82 (t of q, J_{CF} = 267.5 Hz, J_{CCF} = 37.3 Hz), 77.98 (pentet, J_{CCF} = 22.8 Hz), 32.23 (t), 31.27 (t), 22.34 (t), 21.94 (t), and 13.83 (q); IR (neat) 3605 m, 3540–3495 m, 2960 s, 2930 s, 2875 m, 2860 m, 1465 m, 1380 m, 1330 s, 1290 w, 1240–1205 vs, 1190–1170 vs, 1145 s, 1130 s, 1070 s, 1050 m, 1015 m, 972 s, 935 m, 858 m, 749 m, 730 s, 700 w, and 672 w cm^{-1}; exact mass M_r calcd for $C_{10}H_{12}F_{10}O$ *m/e* (M – H) 337.0649, found 337.0647.

Anal. Calcd for $C_{10}H_{12}F_{10}O$: C, 35.51; H, 3.58. Found: C, 35.59; H, 3.65.

1,1,1,2,2,4,4,5,5,5-Decafluoro-3-hydroxy-3-(phenylmethyl)pentane: ^{1}H NMR ($CDCl_3$) δ 7.41–7.38 (m, 3 H), 7.35–7.26 (m, 2 H), 3.43 (s, 2 H), and 2.85 (s, 1 H, exchangeable with deuterium oxide); ^{13}C NMR ($CDCl_3$) δ 131.43 (d), 130.33 (s), 129.21 (d), 128.63 (d), 118.76 (q of t, J_{CF} = 288.0 Hz, J_{CCF} = 35.5 Hz), 113.82 (t of q, J_{CF} = 267.5 Hz, J_{CCF} = 37.3 Hz), 77.76 (pentet, J_{CCF} = 23.8 Hz), and 35.42 (t); IR (neat) 3525 m, 3090w, 3065 w, 3035 w, 1606 w, 1585 vw, 1498 m, 1456 m, 1445 w, 1393 w, 1372 m, 1332 s, 1298 w, 1230–1200 vs, 1190–1165 vs, 1136 s, 1090 s, 1070 s, 1040 s, 1027 m, 960 s, 950 s, 922 s, 910 w, 845 w, 792 w, 760 s, 744 s, 724 s, and 698 s cm^{-1}; exact mass M_r calcd for $C_{12}H_8F_{10}O$ *m/e* 358.0415, found 358.0416.

Anal. Calcd for $C_{12}H_8F_{10}O$: C, 40.24; H, 2.25. Found: C, 40.38; H, 2.33.

4-(Methylthio)-1,1,1,2,2-pentafluorobutan-3-one: ^{1}H NMR ($CDCl_3$) δ 3.51 (s, 2 H) and 2.11 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 186.96 (t, J_{CCF} = 25.9 Hz), 117.84 (q of t, J_{CF} = 286.8 Hz, J_{CCF} = 34.1 Hz), 107.16 (t of q, J_{CF} = 268.2 Hz, J_{CCF} = 38.7 Hz), 37.62 (t), and 15.52 (q); IR (neat) 2985 w, 2923 m, 2900 vw, 2835 w, 1762 s, 1740 vs, 1440 m, 1430 m, 1415 m, 1375 w, 1367 s, 1335 s, 1284 s, 1240–1190 vs, 1150 vs, 1100 s, 1080 s, 990 s, 971 s, 941 s, 873 w, 840 w, 750 m, 710 m, and 680 m cm^{-1}; exact mass M_r calcd for $C_5H_5F_5SO$ *m/e* 207.9981, found 207.9982.

Anal. Calcd for $C_5H_5F_5SO$: C, 28.85; H, 2.42. Found: C, 28.93; H, 2.42.

1,1,1,2,2-Pentafluoro-3-(3-pyridyl)propan-3-one: ^{1}H NMR ($CDCl_3$) δ 9.28 (s, 1 H), 8.92 (d, 1 H, J = 4.9 Hz), 8.36 (d, 1 H, J = 8 Hz), and 7.54 (d of d, 1 H, J = 4.9 and 8 Hz); ^{13}C NMR ($CDCl_3$) δ 182.58 (t, J_{CCF} = 27.6 Hz), 155.38 (d), 151.05 (t of d, J_{CCCCF} = 4.2 Hz), 137.22 (t of d, J_{CCCCF} = 2.7 Hz), 126.99 (s), 123.90 (d), 117.77 (q of t, J_{CF} = 286.6 Hz, J_{CCF} = 33.6 Hz), and 108.36 (t of q, J_{CF} = 268.3 Hz, J_{CCF} = 37.8 Hz); IR (neat) 3050 w, 1710 s, 1585 s, 1474 w, 1420 m, 1354 m, 1330 m, 1284 s, 1230–1210 vs, 1200 s, 1168 s, 1132 s, 1080 s, 1050 m, 1030 s, 1000 w, 895 s, 860 s, 810 m, 744 s, and 682 s cm^{-1}; exact mass M_r calcd for $C_8H_4F_5NO$ *m/e* 225.0213, found 225.0207.

Anal. Calcd for $C_8H_4F_5NO$: C, 42.68; H, 1.79. Found: C, 42.67; H, 1.85.

1,1,1,2,2-Pentafluoro-3-(2-pyridyl)propan-3-one: ^{1}H NMR ($CDCl_3$) δ 8.82 (d, 1 H, J = 3.9 Hz), 8.14 (d, 1 H, J = 7.0 Hz), 7.94 (d of d, 1 H, J = 7.7 and 7.0 Hz), and 7.61 (d of d, 1 H, J = 7.7 and 3.9 Hz); ^{13}C NMR ($CDCl_3$) δ 183.12 (t, J_{CCF} = 25.5 Hz), 149.73 (d), 149.48 (s), 137.31 (d), 128.75 (d), 125.16 (d), 118.26 (q of t, J_{CF} = 286.9 Hz, J_{CCF} = 33.7 Hz), and 108.91 (t of q, J_{CF} = 270.1 Hz, J_{CCF} = 37.7 Hz); IR (neat) 3060 w, 1725 s, 1586 s, 1470 w, 1440 m, 1410 w, 1355 s, 1330 m, 1315 m, 1303 m, 1288 m, 1250 s, 1230 vs, 1220 vs, 1180 vs, 1162 s, 1148 s, 1091 m, 1081 s, 1062 m, 1046 m, 1040 m, 994 m, 975 w, 912 s, 864 s, 800 m, 780 w, 745 s, 739 s, 710 m, 682 s, and 612 m cm^{-1}; exact mass M_r calcd for $C_8H_4F_5NO$ *m/e* 225.0213, found 225.0204.

Anal. Calcd for $C_8H_4F_5NO$: C, 42.68; H, 1.79. Found: C, 42.66; H, 1.85.

3-Hydroxy-1,1,1,2,2-pentafluoro-4-(2-pyridyl)but-3-ene:[22] ^{1}H NMR ($CDCl_3$) δ 8.05 (d, 1 H, J = 5.8 Hz), 7.72 (m, 1 H), 7.10 (d, 1 H, J = 8.5 Hz), 7.03 (t, 1 H, J = 5.8 Hz), and 5.85 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 164.50 (t, J_{CCF} = 24.3 Hz), 155.63 (s), 139.34 (d), 138.30 (d), 122.41 (d), 118.85 (q of t, J_{CF} = 286.8 Hz, J_{CCF} = 36.9 Hz), 117.85 (d), 108.91 (t of q, J_{CF} = 258.8 Hz, J_{CCF} = 37.2 Hz), and 90.98 (d); IR (KBr disk) 3530–3420 w (broad), 3120 w, 2920 w, 1640 s, 1600 s, 1588 s, 1520 m, 1475 w, 1439 m, 1415 w, 1390 w, 1342 m, 1330 m, 1267 w, 1230 m, 1220 m, 1205 s, 1196 s, 1160 s, 1120 m, 1082 w, 1015 s, 1000 w, 985 w, 930 w, 880 m, 866 w, 818 m, 780 s, 749 m, 735 w, 727 w, 712 m, 695 w, 645 w, 603 w, 585 w, 565 w, and 506 w cm^{-1}; exact mass M_r calcd for $C_9H_6F_5NO$ *m/e* 239.0369, found 239.0359.

Anal. Calcd for $C_9H_6F_5NO$: C, 45.20; H, 2.53. Found: C, 45.39; H, 2.67.

4,4-Dimethyl-3-hydroxy-1,1,1,2,2-pentafluoro-3-pentafluoroethylpentane: ^{1}H NMR ($CDCl_3$) δ 2.84 (s, 1 H, exchangeable with deuterium oxide), and 1.29 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 118.86 (q of t, J_{CF} = 288.5 Hz, J_{CCF} = 35.4 Hz), 116.10 (t of q, J_{CF} = 270.55 Hz, J_{CCF} = 37.1 Hz), 85.43 (pentet, J_{CCF} = 23.0 Hz), 40.94 (s), and 27.34 (q); IR (neat) 3630 m, 3020 w, 2990 w, 2970 w, 2930 w, 2900 w, 1493 w, 1480 w, 1450 vw, 1420 w, 1390 w, 1330 m, 1313 m, 1300 w, 1225 s, 1210 s, 1182 s, 1165 s, 1128 m, 1109 m, 1084 m, 1070 w, 1042 m, 1030 m, 1012 m, 930 m, 900 m, 887 w, 845 w, 830 m, 795 w, 744 m, 725 s, and 710 w cm^{-1}; exact mass M_r calcd for $C_9H_{10}F_{10}O$ *m/e* (M – CH_3) 309.0337, found 309.0338.

Anal. Calcd for $C_9H_{10}F_{10}O$: C, 33.34; H, 3.11. Found: C, 33.46; H, 3.23.

3-Cyclohexyl-1,1,1,2,2,4,4,5,5,5-decafluoro-3-hydroxypentane: ^{1}H NMR ($CDCl_3$) δ 2.88 (s, 1 H, exchangeable with deuterium oxide), 2.08–1.95 (m, 3 H), 1.89–1.86 (m, 2 H), 1.79–1.72 (m, 1 H), 1.60–1.36 (m, 2 H), and 1.34–1.19 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 119.05 (q of t, J_{CF} = 288.4 Hz, J_{CCF} = 36.2 Hz), 114.89 (t of q, J_{CF} = 268.3 Hz, J_{CCF} = 36.8 Hz), 80.00 (pentet, J_{CCF} = 22.9 Hz), 46.10 (d), 28.10 (t), 27.74 (t), and 26.56 (t); IR (neat) 3630 m, 2960 m, 2940 m, 2865 m, 1460 m, 1355 m, 1335 m, 1328 s, 1285 w, 1225–1210 s, 1180 s, 1160 s, 1148 s, 1122 s, 1102 m, 1082 w, 1060 w, 1040 m, 1021 m, 949 m, 900 m, 858 m, 837 m, 802 w, 752 m, 736 s, and 725 w cm^{-1}; exact mass M_r calcd for $C_{11}H_{12}F_{10}O$ *m/e* (M – H) 349.0650, found 349.0655.

Anal. Calcd for $C_{11}H_{12}F_{10}O$: C, 37.72; H, 3.45. Found: C, 37.81; H, 3.58.

Cyclohexyl pentafluoroethyl ketone: ^{1}H NMR ($CDCl_3$) δ 2.91 (t, 1 H, J = 10.8 Hz), 1.87 (t, 4 H, J = 14.4 Hz), 1.72 (m, 1 H), 1.50–1.19 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 197.68 (t, J_{CCF} = 25.5 Hz), 118.16 (q of t, J_{CF} = 286.7 Hz, J_{CCF} = 34.2 Hz), 107.44 (t of q, J_{CF} = 267.3 Hz, J_{CCF} = 37.7 Hz), 45.96 (d), 28.29 (t), 25.58 (t), and 25.38 (t); IR (neat) 2940 s, 2865 m, 1751 s, 1455 m, 1381 m, 1338 s, 1255 w, 1230–1220 s, 1200 s, 1168 s, 1140 s, 1115 m, 1075 m, 1050 w, 1020 w, 955 m, 938 s, 920 w, 892 w, 850 w, 800 w, 780 w, and 720 s cm^{-1}; exact mass M_r calcd for $C_9H_{11}F_5O$ *m/e* 230.0730, found 230.0742.

Anal. Calcd for $C_9H_{11}F_5O$: C, 46.96; H, 4.82. Found: C, 47.17; H, 4.93.

Reaction of Ethyl Benzoate with (Pentafluoroethyl)lithium at –110 °C. A 100-mL, round-bottomed, three-necked flask was charged with 1.00 g (6.66 mmol) of ethyl benzoate, 40 mL of anhydrous diethyl ether, and 9.26 g (37.7 mmol) of pentafluoroethyl iodide at –110 °C under a dry nitrogen atmosphere. To the stirred reaction mixture was added 21.3 mL of a 1.5 M solution of methyllithium/lithium bromide solution (32 mmol) in diethyl ether. The reaction mixture was stirred for 3 h at this temperature and was then poured into a separatory funnel containing 80 mL of 1 N aqueous hydrochloric acid solution and 25 mL of diethyl ether. After the layers were shaken and separated, the aqueous layer was extracted with a further 50 mL of diethyl ether. The combined ethereal extracts were dried over anhydrous sodium sulfate and filtered, the solvent was removed on a rotary evaporator, and the residue was distilled under reduced pressure. Discoloration due to the presence of iodine was observed. Therefore the product was dissolved in 50 mL of diethyl ether and washed consecutively with 50 mL of a saturated aqueous solution of sodium thiosulfate and 50 mL of water. The ethereal solution was dried over anhydrous sodium sulfate and filtered, and the solvent was removed on a rotary evaporator. Distillation gave 1.09 g (74%) of 1,1,1,2,2-pentafluoropropiophenone: bp 76–78 °C (29 mm) (lit.[26] bp 161.2 °C); ^{1}H NMR (CDCl$_3$) δ 8.09 (d, J = 7.6 Hz, 2 H), 7.72 (d of d, J = 7.6 and 7.7 Hz, 1 H), 7.55 (t, J = 7.7 Hz, 2 H); ^{13}C NMR (CDCl$_3$) δ 183.19 (t, J_{CCF} = 26.8 Hz), 135.56 (d), 131.01 (s), 130.15 (d), 129.10 (d), 118.05 (q of t, J_{CF} = 286.6 Hz, J_{CCF} = 33.3 Hz), 108.70 (t of q, J_{CF} = 268.6 Hz, J_{CCF} = 37.2 Hz); IR (neat) 3070 vw, 1716 s, 1610 m, 1592 w, 1460 m, 1362 m, 1335 m, 1318 w, 1282 m, 1235–1215 s, 1175 s, 1140 s, 1080 s, 1049 m, 1033 w, 1008 w, 905 m, 869 s, 792 w, 750 s, 718 s, 685 m, 670 m cm^{-1}; exact mass M_r calcd for $C_9H_5F_5O$ m/e 224.0260, found 224.0273.

Low-Temperature Quenching with Trimethylsilyl Chloride of the Reaction of Ethyl Phenylacetate with (Pentafluoroethyl)lithium. A. Warmed to Room Temperature Directly. A 50-mL, round-bottomed, three-necked flask was charged with 0.15 g (0.91 mmol) of ethyl phenylacetate, 1.40 g (5.69 mmol) of pentafluoroethyl iodide, and 20 mL of anhydrous diethyl ether at −78 °C under a dry nitrogen atmosphere. To the stirred solution was added 3 mL of a 1.5 M solution of methyllithium/lithium bromide (4.5 mmol) in diethyl ether. The reaction mixture was stirred for 30 min at this temperature, and 2 mL (3.5 molar excess relative to pentafluoroethyllithium) of trimethylsilyl chloride was added. The cold bath was immediately removed, and the reaction mixture was allowed to warm to room temperature and stirred for a further 10 h. The reaction mixture was poured into a separatory funnel containing 60 mL of a 1 N aqueous hydrochloric acid solution and 30 mL of diethyl ether. After the layers were shaken and separated, the aqueous layer was further extracted with 30 mL of diethyl ether, and the combined extracts were dried over anhydrous sodium sulfate. Nonane (0.18 g) was then added as an internal standard, and GLC analysis (OV101 capillary) showed an 81% yield of the trimethylsilyl enol ether **5**, a 15% yield of the pentafluoroethyl-substituted ketone, and a 2.5% yield of the corresponding bis(pentafluoroethyl)-substituted tertiary carbinol.

1,1,1,2,2-Pentafluoro-4-phenyl-3-[(trimethylsilyl)oxy]-but-3-ene (15) was isolated in pure form by filtration, removal of the solvent from the filtrate by using a rotary evaporator, and distillation of the residue [bp 66–69 °C (2 mm)] followed by preparative-scale GLC (10 ft OV101, 160 °C): ^{1}H NMR (CDCl$_3$) δ 7.56 (d, 2 H, J = 7.8 Hz), 7.39–7.29 (m, 3 H), 6.32 (s, 1 H), and 0.16 (s, 9 H); ^{13}C NMR (CDCl$_3$) δ 138.21 (t, J_{CCF} = 24.3 Hz), 133.10 (s), 129.29 (d), 128.40 (d), 128.15 (d), 118.90 (q of t, J_{CF} = 287.2 Hz, J_{CCF} = 37.9 Hz), 115.15 (t of d, J_{CCCF} = 5.1 Hz), 110.55 (t of q, J_{CF} = 255.6 Hz, J_{CCF} = 37.9 Hz), and 0.29 (q); IR (neat) 3090 w, 3062 w, 3030 w, 2965 m, 2900 w, 1665 s, 1500 m, 1450 m, 1430 w, 1415 w, 1380 s, 1330 s, 1300 w, 1258 vs, 1215 vs, 1200 vs, 1159 vs, 1100 s, 1075 m, 1041 m, 1030 s, 1017 vs, 1000 m, 922 m, 890 s, 842 s, 750 s, 735 s, 720 m, 690 s, 662 m, and 645 w cm^{-1}; exact mass M_r calcd for $C_{13}H_{15}F_5OSi$ m/e 310.0812, found 310.0814.

Anal. Calcd for $C_{13}H_{15}F_5OSi$: C, 50.31; H, 4.87. Found: C, 50.12; H, 4.84.

B. Low Temperature Maintained. A 50-mL, round-bottomed, three-necked flask was charged with 0.34 g (2.07 mmol) of ethyl phenylacetate, 15 mL of anhydrous diethyl ether, 3.47 g (14.1 mmol) of pentafluoroethyl iodide, and 0.38 g of dodecane (as an internal standard) at −78 °C under a dry nitrogen atmosphere. To the stirred solution was then added 6.5 mL (10.4 mmol) of a 1.6 M solution of methyllithium/lithium bromide complex in diethyl ether. The reaction mixture was stirred for 0.5 h at this temperature and GLC analysis (OV101 capillary) of an acid-quenched aliquot after this time showed an 81% yield of **8** and a 14% yield of **16**. An excess (4 mL) of trimethylsilyl chloride was then added, and the reaction mixture was stirred for a further 8 h at −78 °C. Analysis of a quenched aliquot at this time showed an 83% yield of **8**, a 15% yield of **16**, and a 1% yield of **15**. The reaction mixture was then allowed to warm to room temperature and stirred for a further 13 h, after which time it was poured into a separatory funnel containing 80 mL of a 1 N aqueous solution of hydrochloric acid and 25 mL of diethyl ether. After the mixture was shaken and the layers were separated, the aqueous layer was extracted with a further 25 mL of diethyl ether. The combined extracts were dried over anhydrous sodium sulfate and GLC analysis showed a 43% yield of **8**, a 16% yield of **16**, and a 41% yield **15**. Reexposure of the product mixture to the acidic workup conditions did not change the product ratio.

Reaction of 1,1,1,2,2-Pentafluoro-4-phenylbutan-3-one with (Pentafluoroethyl)lithium. A 50-mL, round-bottomed, three-necked flask was charged with 10 mL of anhydrous diethyl ether and 2.03 g (8.3 mmol) of pentafluoroethyl iodide at −78 °C under a dry nitrogen atmosphere. To the stirred solution was added 5 mL (7.5 mmol) of an ethereal solution of methyllithium/lithium bromide (1.5 M), and the reaction mixture was stirred for 5 min. A solution of 1,1,1,2,2-pentafluoro-4-phenylbutan-3-one (0.15 g, 0.6 mmol) in 5 mL of anhydrous diethyl ether was added, and the reaction mixture was stirred for 15 min before being poured into a separatory funnel containing 60 mL of a 1 N hydrochloric acid solution and 25 mL of diethyl ether. After the layers were shaken and separated, the aqueous layer was extracted with an additional 50 mL of diethyl ether. The combined ethereal extracts were dried over anhydrous sodium sulfate, and 0.28 g of dodecane (as internal GLC standard) was then added. GLC analysis (OV101 capillary) indicated the presence of 168 mg (80% yield) of the corresponding bis(pentafluoroethyl)-substituted carbinol **16** together with 7.5 mg (5%) of unreacted **8** remaining.

Reaction of 1,1,1,2,2-Pentafluoro-4-phenylbutan-3-one with Lithium Ethoxide Followed by Trimethylsilyl Chloride Quenching. A 50-mL, round-bottomed, three-necked flask was charged with 0.62 g (2.6 mmol) of 1,1,1,2,2-pentafluoro-4-phenylbutan-3-one and 20 mL of anhydrous diethyl ether under a dry nitrogen atmosphere. To the stirred reaction mixture was added 0.30 g (5.8 mmol) of lithium ethoxide, and stirring was continued for 30 min at room temperature. Trimethylsilyl chloride (1 mL, 7.9 mmol) was then added, and stirring was continued for an additional 30 min. The reaction mixture was then poured into a separatory funnel containing 60 mL of a 1 N hydrochloric acid solution and 20 mL of diethyl ether. After the layers were shaken and separated, the aqueous layer was extracted with a further 30 mL of diethyl ether. The combined ethereal extracts were dried over anhydrous sodium sulfate, and 0.48 g of nonane (as internal GLC standard) was added. GLC analysis (OV101 capillary) indicated the presence of 0.31 g (50% recovery) of the starting **8** and 0.36 g (88% yield based on 50% conversion) of 1,1,1,2,2-pentafluoro-4-phenyl-3-[(trimethylsilyl)oxy]but-3-ene (**15**).

Preparation of 1,1,1,2,2-Pentafluorooctan-3-one (25). A 50-mL, round-bottomed, three-necked flask was charged with 0.18 g (1.3 mmol) of ethyl hexanoate, 15 mL of anhydrous diethyl ether, and 1.89 g (7.7 mmol) of pentafluoroethyl iodide at −78 °C under a dry nitrogen atmosphere. To the stirred reaction mixture was added 4.2 mL (6.3 mmol) of a 1.5 M solution of methyllithium/lithium bromide in diethyl ether.[27] After being stirred for 30 min at this temperature, the reaction mixture was poured into a separatory funnel containing 30 mL of a 1 N aqueous solution of hydrochloric acid and 25 mL of diethyl ether. After the layers were shaken and separated, the aqueous layer was extracted with a further 25 mL of diethyl ether. The combined ethereal extracts were dried over anhydrous sodium sulfate, and 0.13 g of decane was added. GLC analysis (OV101 capillary) indicated the presence of 0.23 g (85%) of ketone **25** and 0.01 g (2%) of the corresponding carbinol **24**.

Compound **25** was isolated in pure form by filtration of the reaction mixture, followed by removal of the solvent from the filtrate by distillation through a 13-cm Vigreaux column, and separation by preparative-scale GLC (OV101, 50 °C, followed by Carbowax, 55 °C): bp 113–115 °C (atmospheric); ^{1}H NMR (CDCl$_3$) δ 2.73 (t, 2 H, J = 7.2 Hz), 1.66 (pentet, 2 H, J = 7.2 Hz), 1.33–1.24 (m, 4 H), 0.89 (t, 3 H, J = 6.9 Hz); ^{13}C NMR (CDCl$_3$) δ 194.42 (t, J_{CCF} = 26.2 Hz), 117.96 (q of t, J_{CF} = 286.4 Hz, J_{CCF}

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(26) Simons, J. H.; Black, W. T.; Clark, R. F. *J. Am. Chem. Soc.* **1953**, *75*, 5621.

(27) This is the limiting reagent and allows for a concentration of (pentafluoroethyl)lithium of 6.3 mmol in 19.2 mL = 0.33 M.

= 34.2 Hz), 107.02 (t of q, J_{CF} = 266.5 Hz, J_{CCF} = 38.1 Hz), 37.36 (d), 30.92 (d), 22.36 (d), 22.11 (d), 13.74 (t); IR (neat) 3500 vw, 2965 s, 2938 s, 2880 m, 2870 m, 1765 vs, 1480–1465 w, 1412 w, 1390–1380 w, 1360 m, 1342 s, 1240–1200 vs, 1172 s, 1140 m, 1128 s, 1100 w, 1070 m, 1040–1030 w, 990 w, 930 m, 895 w, 840 vw, 757 w, 736 w, 720 m cm^{-1}; exact mass M_r calcd for $C_8H_{11}F_5O$ *m/e* (M + H, CI, CH_4 reagent gas) 219.0808, found 219.0804.

Anal. Calcd for $C_8H_{11}F_5O$: C, 44.04; H, 5.08. Found: C, 44.44; H, 5.14.

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Supplementary Material Available: ORTEP drawing of 3, tables of atomic coordinates and thermal parameters of nonhydrogen atoms of 3, general temperature factor expressions, least-squares planes, torsional angles in degrees, and positional parameters (including hydrogens) and their standard deviations (9 pages). Ordering information is given on any current masthead page.

A Chiral Stationary Phase Derived from (*R*,*R*)-Tartramide with Broadened Scope of Application to the Liquid Chromatographic Resolution of Enantiomers

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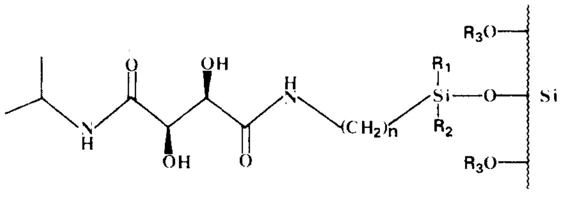
An understanding of the retention process of solute enantiomers on a chiral stationary phase (CSP) would indicate the importance of eliminating the nonenantioselective, i.e., solute–silanol, interaction that occurs in this process. For clarification of this matter, a CSP in which a (*R*,*R*)-*N*,*N*′-dialkyltartramide derivative is linked to the silica gel surface via 11 methylene units and the remaining silanol groups are trimethylsilylated was synthesized. This CSP was found capable of chiral recognition of broad categories of enantiomers containing α- or β-hydroxy carbonyl, α-amino acid, β-amino alcohol, primary amine derivatives, barbiturates, glutarimide, α-hydroxy ketoximes, carbinols, 1,2-diols, and bi-β-naphthol. The driving force to bring about enantioselective association is ascribable to hydrogen bonding. The effects of a reduction in the number of remaining silanol groups on CSP and a long alkyl chain as a linkage of the tartramide moiety to CSP are discussed on the basis of retentivity of enantiomers.

The chiral-stationary-phase (CSP) method for the liquid chromatograhic resolution of enantiomers has gained general acceptance owing to its ease of operation and preparative-scale applications. However, among a number of CSPs developed to date, those with a general scope of application are few.[1-3] The present study describes a new type of CSP derived from (*R*,*R*)-tartramide (CSP 1) on which broad categories of enantiomers are readily resolved.



CSP 1, $R_1 = R_2 = CH_3$; $R_3 = Si(CH_3)_3$; $n = 11$

CSP 2, $R_1 = R_2 = CH_3$; $R_3 = H$; $n = 11$

CSP 3, $R_1 = OH$; $R_2 = O\text{—}Si$; $R_3 = H$; $n = 3$

The performance of CSP is determined by the efficiency of the resulting column and scope and magnitude of chiral recognition. Of these two factors, the later depends primarily on the intrinsic ability of the resolving agent incorporated into CSP. We recently reported that (*R*,*R*)-*N*,*N*′-diisopropyltartramide (DIPTA)[4] functions as a broadly applicable chiral-mobile-phase additive (CMPA) in silica gel chromatography. This CMPA recognizes the molecular chirality of enantiomers through its dual hydrogen-bond association and is capable of resolving enantiomers containing α- or β-hydroxy carboxylic acid, β-hydroxy ketone, β-amino alcohol, α-amino acid, α-hydroxy ketoxime, 1,2-diol derivatives, and bi-β-naphthol. Successful resolution using (*R*,*R*)-DIPTA as a CMPA indicates that the tartramide derivative holds promise for being incorporated into CSP. CSPs are generally prepared by a surface modification of a porous silica gel with an appropriate resolving agent since the methods for this are well established[5] and, most importantly, a high efficiency of the resulting column is possible. At our initial stage of the developement of a CSP derived from tartramide, the tartramide derivative was linked to the silica gel surface via a propylene unit through reaction of the corresponding triethoxysilyl derivative with a silica gel (CSP 3).[6] Although a series of *N*-*tert*-butyl-β-hydroxy carboxamides were resolved well on this phase, its scope of application was not equal to that obtained by using (*R*,*R*)-DIPTA as a CMPA.

The unsatisfactory results of our initially designed CSP are ascribed to remaining silanol groups on CSP. The remaining silanol groups interact with the solute enantiomers by forming hydrogen bonds in competition with the chiral moiety of CSP. In such a case, the separation

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