New Method for Trifluoromethylation of Enolate Anions and Applications to Regio-, Diastereo- and Enantioselective Trifluoromethylation

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Assessment was made of the effectiveness of different boron Lewis acids in mediating the trifluoromethylation of reactive enolate anions with *S*- and *Se*-(trifluoromethyl)chalcogen salts. Treatment of potassium or lithium enolates derived *in situ* from carbonyl compounds or enol trimethylsilyl ethers with *S*-(trifluoromethyl)dibenzothiophenium triflate (**1**) in the presence of 2-phenyl-1,3,2-benzodioxaborole (**4**) produced trifluoromethylated carbonyl compounds in high yields. In this manner, various α-CF_3 ketones, γ-CF_3-α,β-unsaturated ketones, and an α-CF_3 ester were synthesized. Perfluorooctylation was similarly conducted using *S*-(perfluorooctyl)dibenzothiophenium triflate and **4**. Thus, a balance of the reactivity of the reactants was essential for these electrophilic perfluoroalkylations. The deprotonation of 2-methylcyclohexanone with $KN(SiMe_3)_2$ followed by trifluoromethylation gave the 6-trifluoromethylated product regioselectively. In the trifluoromethylation of potassium enolate **16** of 4,4a,5,6,7,8-hexahydro-4a-methyl-2(3*H*)-naphthalenone, the use of bulky 2-mesitylphenanthro[9,10-*d*]-1,3,2-dioxaborole (**15**) led to the diastereoselective formation of the thermodynamically less stable CF_3-isomer **17β**. For enantioselective trifluoromethylation, optically active (*S*)-4-phenyldinaphtho[2,1-*d*:1′,2′-*f*][1,3,2]dioxaborepin (**19**) and its 3,3′-diphenyl derivative **20** were synthesized. The trifluoromethylation of the potassium enolate of propiophenone with **1** in the presence of **20** afforded optically active α-CF_3-propiophenone in 45% ee yield. Thus, a new and versatile method for selective trifluoromethylation has been developed.

Introduction

The introduction of a trifluoromethyl group into an organic molecule often induces significant changes in its chemical, physiological, or physical nature, because of the trifluoromethyl group's high electronegativity, stability, and lipophilicity.[1] Thus, trifluoromethylated organic compounds are becoming increasingly important to the development of more effective medicines[2] and agricultural chemicals,[3] and new materials such as liquid crystals.[4] Currently available methods for the synthesis of trifluoromethylated carbonyl compounds from the parent carbonyl compounds require multiple steps, and proceed via the trifluoromethylation of enamines,[5] enol alkyl,[6] silyl or germyl ethers,[7] enol esters,[8] or ketene silyl acetals.[7] The radical-initiated trifluoromethylation of enolate anions of *N*-acyloxazolidinones with a large excess of trifluoromethyl iodide has recently been reported.[9]

We have developed a new class of electrophilic trifluoromethylating agents, *S*-, *Se*-, and *Te*-(trifluoromethyl)-dibenzothio-, -seleno-, and -tellurophenium salts, which vary in reactivity and which can be selected based on the nucleophilicity of the substrate.[10] The trifluoromethylation of enolate anions derived *in situ* from ketones with a base, using any of our electrophilic trifluoromethylating agents was unsuccessful with the exception of an enolate anion derived from 2-methyl-1-indanone, which has a tertiary α-carbon.[11] The reactivity of the enolate anions may have been too great for these trifluoromethylating agents. We therefore moderated the reactivity of the enolate anions by complexation to various boron Lewis acids to provide a more suitable match between the nucleophilicity of the enolate and the electrophilicity of the trifluoromethylating agent. A new and versatile method for the regio-, diastereo-, and enantioselective trifluoromethylation of enolate anions by a suitable combination of trifluoromethylating agents and boron Lewis acids is presented in this paper.

Results and Discussion

The potassium enolate of 1-indanone was allowed to react with *S*-(trifluoromethyl)dibenzothiophenium triflate

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(1) (a) *Organic Fluorine Chemistry*; Sheppard, W. A., Sharts, C. M., Eds.; Benjamin Inc.: New York, 1969. (b) Chambers, R. D. *Fluorine in Organic Chemistry*; John Wiley & Sons: New York, 1973. (c) Ishikawa, N.; Kobayashi, Y. *Fusso no Kagobutu*; Kodansha Ltd.: Tokyo, 1979.

(2) (a) *Biomedicinal Aspects of Fluorine Chemistry*; Filler, R., Kobayashi, Y., Eds.; Kodansha Ltd.: Tokyo, 1982. (b) Kumadaki, I. *J. Synth. Org. Chem., Jpn.* **1984**, *42*, 786. (c) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123. (d) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; John Wiley & Sons, Inc.: New York, 1991. (e) *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications*; Filler, R., Kobayashi, Y., Yagupolskii, L. M., Eds.; Elsevier: Amsterdam, 1993.

(3) (a) Yoshioka, H.; Nakayama, C.; Matsuo, N. *J. Synth. Org. Chem., Jpn.* **1984**, *42*, 809. (b) *90 Nendai no Fussokei Seirikassei Bussitu. Kaihatu to Oyo*; Ishikawa, N., Ed.; CMC, Ltd.: Tokyo, 1990.

(4) Nohira, H. *J. Synth. Org. Chem., Jpn.* **1991**, *49*, 467.

(5) (a) Cantacuzène, D.; Wakselman, C.; Dorme, R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1365. (b) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186.

(6) (a) Uneyama, K.; Kitagawa, K. *Tetrahedron Lett.* **1991**, *32*, 375. (b) Uneyama, K.; Kanai, M. *Ibid.* **1991**, *32*, 7425.

(7) (a) Miura, K.; Taniguchi, M.; Nozaki, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1990**, *31*, 6391. (b) Miura, K.; Takeyama, Y.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1542.

(8) Langlois, B. R.; Laurent, E.; Roidot, N. *Tetrahedron Lett.* **1992**, *33*, 1291.

(9) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1993**, *34*, 2169.

(10) (a) Umemoto, T.; Ishihara, S. *Tetrahedron Lett.* **1990**, *31*, 3579. (b) Umemoto, T.; Ishihara, S. *J. Am. Chem. Soc.* **1993**, *115*, 2156.

(11) The lithium enolate of 2-methyl-1-indanone generated with LDA was treated with **1** to give 2-methyl-2-(trifluoromethyl)-1-indanone in 51% yield.[10b] In this reaction, CF_3H was formed in ca. 17% or more yield.

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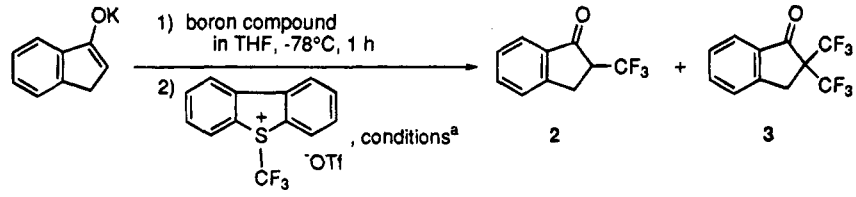
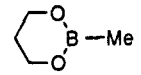
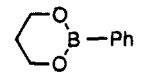
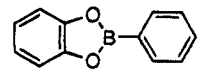
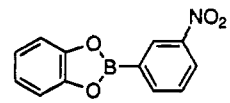
Table 1. Trifluoromethylation of Potassium Enolate of 1-Indanone

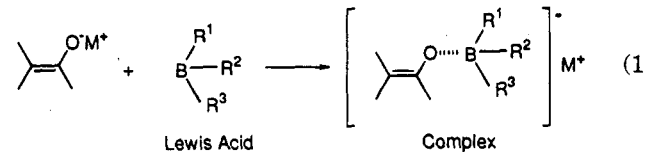


run[b]	boron compound	conditions temp(°C)	time(h)	yield(%)[c] 2	3	CF_3H[d]	remaining 1 (%)[c]
1	none	-78	1	0.8	8	17	0
2	Et_3B[e]	-78	1	47	10	13	0
3		-78	1	25	3	23	7
4	Ph_3B	-78	1	61	4	3	18
5		-78	1	44	1	15	6
6	$(MeO)_3B$	-78 → 0	2.5	36	trace	11	1
7	 4	-78 → 0	2.5	85(76)	0	trace	7
8	 5	-78 → 0	2.5	56	0	trace	32

[a] These conditions are shown in this table. [b] Potassium enolate of 1-indanone was generated *in situ* by treatment of 1-indanone with KH in THF at rt for 1 h. The mol ratio of 1-indanone/KH/**1** was 1.05/1.0/1.1 in run 1. Mol ratios of 1-indanone/KH/boron compound/**1** were 1.1/1.05/1.2/1.0 in runs 2–5, and 1.2/1.2/1.2/1.0 in runs 6–8. [c] Yields were determined by ^{19}F NMR relative to an internal standard (benzotrifluoride). The value in parentheses (run 7) is an isolated yield. [d] Yields of CF_3H were not accurate because gaseous CF_3H escaped from the reaction mixture. [e] In this case, at rt, Et_3B (1.0 M in THF) was added dropwise to a solution of the potassium enolate in THF and the reaction mixture was stirred for 1 h.

(**1**) in the absence of a boron compound. The desired α-trifluoromethylated ketone **2** was obtained only in trace amounts (0.8%); bis(trifluoromethyl) ketone **3** was formed in 8% yield (run 1 in Table 1). The potassium enolates of 1-indanone and cyclohexanone were then treated with **1** in the presence of various boron compounds differing in Lewis acidity. The results are shown in Tables 1 and 2. The results obtained with *S*-(trifluoromethyl)dibenzothiophenium tetrafluoroborate (**7**), *Se*-(trifluoromethyl)-dibenzoselenophenium triflate (**8**), and *S*-(trifluoromethyl)-diphenylsulfonium triflate (**9**) are shown in Table 2. Using triflate **1** with borole **4**, enolates were readily trifluoromethylated to give α-trifluoromethyl ketones **2** and **6** in high yields and byproduct formation (CF_3H and bis(trifluoromethyl) ketones) was completely suppressed (run 7 in Table 1 and run 3 in Table 2). With tetrafluoroborate **7** instead of triflate **1**, the yield of **6** decreased to 65%, possibly owing to the low solubility of **7** in THF (run 5 in Table 2).

Enolate anions should complex with boron Lewis acids as shown in eq 1. The nucleophilicity of the resulting complexes should depend on the Lewis acidity of the boron compound employed. The Lewis acidity of the

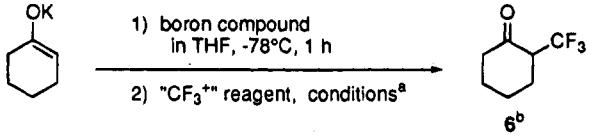


(1)

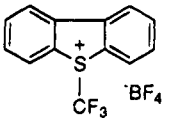
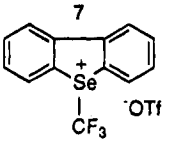
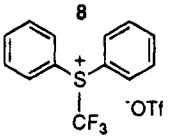
boron compounds employed in this study should increase in the order of Et_3B < MeB(-$OCH_2CH_2CH_2O$-) < Ph_3B < PhB(-$OCH_2CH_2CH_2O$-) < $(MeO)_3B$ < **4** < **5**, based on reported ^{13}C NMR data of boron complexes with pyridine[12] and the inductive effect of the boron substituents (R^1–R^3). The power of the trifluoromethylating agents decreases in the order, **1** > **8** > **9**.[10] The yields of the products may not be correlated linearly with the Lewis acidity order, because different types of boron compounds were used. However, with each type of boron compounds, yield clearly correlates with the Lewis acidity order. Thus, on going from Et_3B to Ph_3B and from MeB(-$OCH_2CH_2CH_2O$-) to PhB(-$OCH_2CH_2CH_2O$-), the yield of **2** increased and that of **3** and CF_3H decreased (Table 1).

(12) Farfán, N.; Contreras, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, 771.

Table 2. Trifluoromethylation of Potassium Enolate of Cyclohexanone



6[b]

run[c]	boron compound	"CF_3^+" reagent	conditions temp(°C)	time(h)	yield(%)[d] 6	CF_3H[e]	remaining "CF_3^+" reagent(%)[d]
1	Et_3B[f]	1	-78	2	5	32	0
2	$(MeO)_3B$[f]	1	-78	1	trace	30	28
3	4	1	-78 → 0	2.5	86(85)	trace	2.5
4	5	1	-78 → 0	2.5	28	trace	59
5	4	 7	-78 → 0	2.5	65	trace	10
6	4	 8	-78 → 0	2.5	48	9	18
7	4	 9	-78 → 0	2.5	48	trace	44

[a] These conditions are shown in this table. [b] See ref, 5a and 8. [c] Potassium enolate of cyclohexanone was generated *in situ* by treatment of cyclohexanone with KH in THF at rt for 1 h. Mol ratios of cyclohexanone/KH/boron compound/"CF_3^+" reagent were 1.0/1.05/1.25/1.0 in run 1, 1.1/1.05/1.1/1.0 in run 2, and 1.2/1.2/1.2/1.0 in runs 3–7. [d] Yields were determined by ^{19}F NMR relative to an internal standard (benzotrifluoride). The value in parentheses (run 3) is an isolated yield. [e] See *d* in Table 1. [f] In this case, at rt, the boron compound (1.0 M in THF) was added dropwise to a solution of the potassium enolate in THF and the reaction mixture was stirred for 40 min.

Borole **4** gave the maximum yields of **2** and **6** and no, or only trace amounts, of byproducts. On going from borole **4** to **5**, the yields of **2** and **6** decreased and the remaining **1** increased (Tables 1 and 2). Thus, the reactivity of complexes of enolates with borole **4** is most suited to the electrophilicity of trifluoromethylating agent **1**. Weaker Lewis acids increased byproduct formation, while more powerful Lewis acids, such as **5**, made trifluoromethylation difficult and a large amount of **1** remained unreacted. Prolonged reaction time caused partial decomposition of **1**. Less powerful trifluoromethylating agents **8** and **9** gave lower yields of **6** and the least powerful **9** gave the lowest conversion; 44% of **9** remained (run 7 in Table 2).

In our previous paper, a bimolecular ionic substitution mechanism was proposed for electrophilic trifluoromethylation.[10b] This successful boron-mediated reaction may be explained by the bimolecular ionic substitution between the trifluoromethylating agents and the complexes of enolates with the boron Lewis acids. Weaker Lewis acids caused increased CF_3H formation, possibly through a CF_3 radical chain reaction initiated by one-electron transfer.

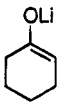
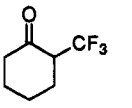
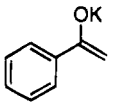
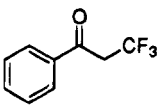
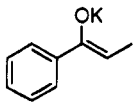
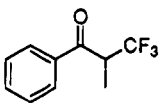
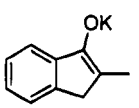
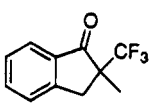
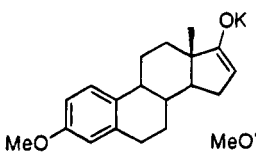
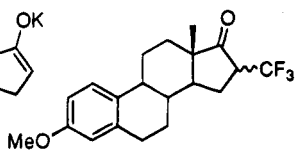
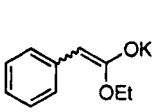
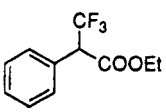
Bistrifluoromethylated product **3** is presumably formed by trifluoromethylation of the initially formed monotrifluoromethylated product **2**. The more acidic α-proton of the mono-CF_3 product **2** is removed by unreacted enolate anion to give the enolate anion of **2**, which reacts with **1** to give the bis-CF_3 product **3**. That **3** was not formed with borole **4** may be explained as follows. The complex of the enolate of 1-indanone with **4** is minimally or incapable of deprotonating **2** and, even if **2** is deprotonated, the complex formed between the enolate of **2** and borole **4** is too low in nucleophilicity to react with **1**. The possible deprotonation of **2** can be excluded because the enantioselective trifluoromethylation of the potassium enolate of propiophenone was successful as is described later. The deprotonation should result in racemization.

Negishi et al.[13] and Rathke et al.[14] found that, in the reaction of the potassium or sodium enolate of cyclohexanone with methyl iodide, the addition of triethylborane greatly decreased the formation of α-dimethylcyclohexanone, so that α-monomethylcyclohexanone was produced in high yield. In that study, the more Lewis acidic trimethyl borate completely prevented methylation.[14] However, the Lewis acidity of trimethyl borate was found to be low enough for the present trifluoromethylation using **1**, since trimethyl borate gave a considerable amount of the byproduct CF_3H (run 6 in Table 1 and run 2 in Table 2).

This method of using trifluoromethylating agent **1** and borole **4** in combination was successfully applied to the

(13) (a) Negishi, E.; Idacavage, M. J. *Tetrahedron Lett.* **1979**, 845. (b) Negishi, E.; Chatterjee, S. *Ibid.* **1983**, *24*, 1341.
(14) Rathke, M. W.; Lindert, A. *Synth. Commun.* **1978**, *8*, 9.

Table 3. Trifluoromethylation of Various Enolates with 1 and Borole 4

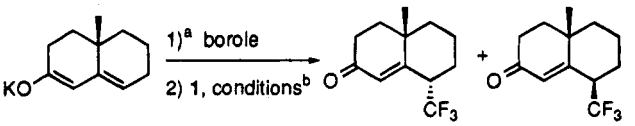
run[a]	enolate	product	yield(%)[b]
1			71
2			92[c] (73)
3			89 (76)
4			79 (76)
5	 10	 11 (α/β = 2/3)[d]	58 (44)
6			40

[a] In all runs, the reactions of enolates with **4** followed by **1** were carried out under the same conditions as in run 7 in Table 1. The lithium enolate in run 1 was generated *in situ* by treatment of the enol trimethylsilyl ether of cyclohexanone with MeLi in THF at rt for 1 h. The potassium enolates in runs 2–6 were generated *in situ* by treatment of the corresponding ketones or ester with KH in THF at rt for 1 h. In run 5, enolate **10** was generated in the presence of HMPA (equimolar to the starting ketone) as an additive. Mol ratios of substrate/base/**4**/**1** were 1.2/1.2/1.2/1.0 for all runs (substrate: the starting ketone, enol trimethylsilyl ether or ester; base: MeLi or KH). [b] Yields were determined by ^{19}F NMR relative to an internal standard (benzotrifluoride). Values in parentheses are isolated yields. [c] In this case, 3-nitrobenzotrifluoride was used as an internal standard for ^{19}F NMR analysis. [d] Isomer ratio.

trifluoromethylation of various potassium or lithium enolates generated *in situ* from the corresponding carbonyl compounds or enol trimethylsilyl ethers. The results are shown in Tables 3 and 4. Enolates of ketones and an α,β-unsaturated ketone, having primary, secondary, or tertiary α-carbons, were monotrifluoromethylated in high yields; no bistrifluoromethylated products could be detected and CF_3H was formed only in trace amounts. As shown with enolates **10** and **16**, trifluoromethylation could be conducted even in the presence of the easily oxidizable amine derivative,[15] HMPA, which was added to facilitate the generation of enolate anions. Reaction of the potassium enolate of ethyl phenylacetate with **1** gave ethyl 2-(trifluoromethyl)phenylacetate in 40% yield (run 6 in Table 3). However, attempts to α-trifluoromethylate enolate anions of other esters, such as methyl 4-phenylbutanoate failed. The nucleophilicity of these ester enolate–Lewis acid complexes must be too high, because CF_3H was formed in large amounts. Perhaps, in the successful reaction of ethyl phenylacetate, the decreased nucleophilicity of the ester enolate–Lewis acid

(15) Triflate **1** was immediately decomposed by easily oxidizable triethylamine even at low temperature (−78 °C).[10b]

Table 4. Diastereoselective Trifluoromethylation of 16 with Boroles 4, 14, and 15



16 17α[c] 17β[c]

run[d]	borole	conditions temp(°C)	conditions time(h)	yield(%)[e]	ratio of α/β isomers[e,f] 17α : 17β
1	**4**	-78 → 0	2.5	81(80)	1 : 2.5
2	**14**	-78 → rt	24	50	1 : 3
3	**15**	-20 → rt	24	51	1 : 4

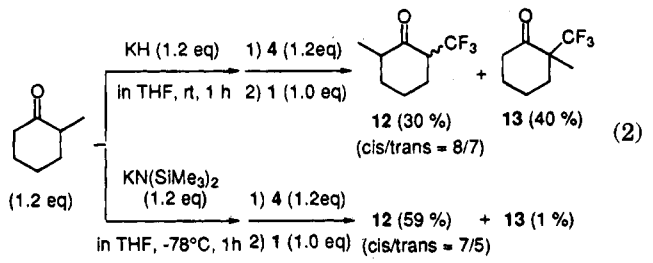
[a] In run 1, borole **4** was added to a solution of **16** in THF at −78 °C and the reaction mixture was stirred at the same temperature for 1 h. In runs 2 and 3, borole **14** or **15** was added to a solution of **16** in THF cooled in an ice bath and the reaction mixtures were stirred at rt for 1 h. [b] These conditions are shown in this table. [c] See ref 10. [d] Potassium enolate **16** was generated *in situ* by treatment of the corresponding α,β-unsaturated ketone with KH in THF at rt for 1 h in the presence of HMPA as an additive. Mol ratios of the ketone/KH/HMPA/borole/**1** were 1.2/1.2/1.2/1.2/1.0 for all runs. [e] Yields and ratios of α/β isomers were determined by ^{19}F NMR relative to an internal standard (benzotrifluoride). The value in parentheses is an isolated yield. [f] Compound **17β** was found to isomerize to the **17α** isomer under acidic conditions. Thus, a 1/2.5 mixture of **17α/17β** (in run 1) changed to a 2.5/1 mixture of **17α/17β** by addition of a small amount of concd hydrochloric acid.

complex, due to conjugation of the enolate with the phenyl ring, is the important factor.

The trifluoromethylation of an enolate anion derived from 2-methylcyclohexanone with KH afforded a 3:4 mixture of 2-methyl-6-(trifluoromethyl)- and 2-methyl-2-(trifluoromethyl)cyclohexanone (**12** and **13**) in 70% yield (eq 2). This was an unexpected result, because the thermodynamic deprotonation of 2-methylcyclohexanone with KH was reported to occur at the 2-position almost exclusively (6-/2-position = 7/93).[13] The minimal regioselectivity in the trifluoromethylation at the 2-position of 2-methylcyclohexanone may be attributable to considerable regioselective scrambling of the enolate, probably due to difficulty in the trifluoromethylation at the crowded 2-position. In contrast, an analogous reaction that involved kinetic deprotonation of 2-methylcyclohexanone at the 6-position using $KN(SiMe_3)_2$[16] gave 59% of **12**, contaminated with a trace (1%) of **13**. High regioselectivity was thus obtained in the kinetically-generated enolate anion which has the less crowded reaction site. This suggests that the crowdedness of the reaction site may be another important factor for the regioselective trifluoromethylation.

A comparison of diastereoselectivity for the present boron-mediated trifluoromethylation of enolate anion **16** and the reported trifluoromethylation[10] of the corresponding enol trimethylsilyl ether with **1** was made. The α/β ratio of products **17α** and **17β** was 1/2.5 for the former reaction and 3.6/1 for the latter reaction. In the boron-mediated reaction, the thermodynamically less stable β-isomer **17β** is the main product. The conformation of the intermediate complex, in which a bulky Lewis acid has complexed with the enolate oxygen from the unhin-

(16) Brown, C. A. *J. Org. Chem.* **1974**, *39*, 3913.

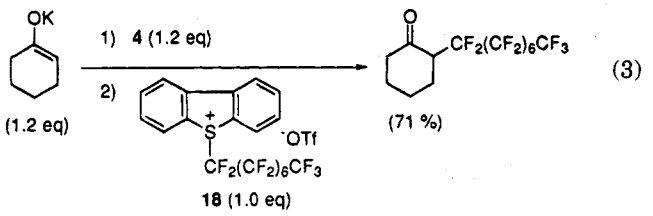


(2)

dered α-face, would force reagent **1** to attack the complex from the less hindered β-face, giving the **17β** isomer predominantly, as shown in Figure 1. The preferential formation of β-CF_3 steroid isomer **11** (α/β = 2/3) can be explained by a similar rationale (run 5 in Table 3).

Assessment was made of the effectiveness of bulky boron compounds **14** and **15** (Figure 2) for preferentially obtaining thermodynamically less stable β-CF_3 isomer **17β**. Borole **14** was synthesized in 83% yield by azeotropic dehydration of catechol and mesityleneboronic acid in toluene under reflux for 12 h. Borole **15** was similarly synthesized in 88% yield from mesityleneboronic acid and 9,10-phenanthrenediol. As shown in Table 4, boroles **14** and **15** gave 1/3 and 1/4 mixtures of **17α/17β** in 50 and 51% yields, respectively. The proportion of the β-isomer thus increases with the bulkiness of the borole. This supports the above explanation of the conformation of the intermediate complexes.

Perfluorooctylation of the potassium enolate anion of cyclohexanone was conducted using *S*-(perfluorooctyl)-dibenzothiophenium triflate (**18**) and borole **4** (eq 3). Thus, other perfluoroalkyl groups than the CF_3 group can be introduced using this methodology. The α-perfluorooctylated cyclohexanone could not be isolated in pure form by silica gel column chromatography due to partial dehydrofluorination. Thus, the fully dehydrofluorinated compound, 2-(perfluorooctylidene)cyclohexanone, was prepared, by treating the product with triethylamine in dichloromethane, and characterized. According to the ^{19}F NMR spectrum, the (perfluorooctylidene)cyclohexanone isolated was a single isomer, probably the thermodynamically stable *Z*-isomer.



(3)

Application of the present method to the enantioselective trifluoromethylation of prochiral potassium enolates using optically active boron compounds was made. The synthesis and reactions of optically active boron Lewis acids have been extensively studied.[17] Since the magnitude of the Lewis acidity is an essential factor for the trifluoromethylation as discussed above, the optically

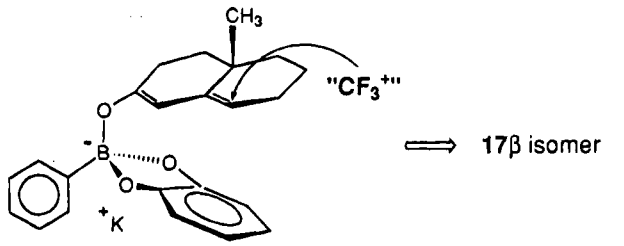


Figure 1.

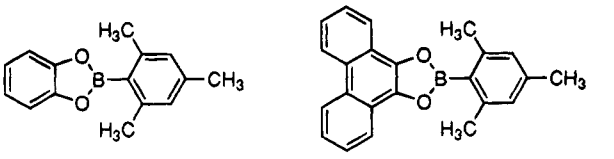


Figure 2.

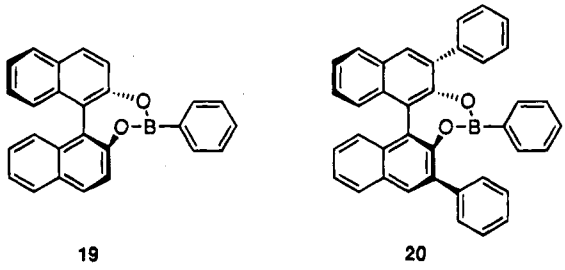


Figure 3.

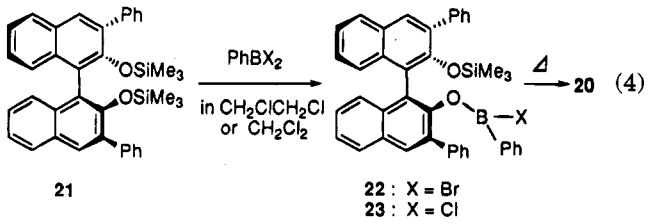
active boron compounds needed for this successful enantioselective trifluoromethylation should require the same skeleton as **4**, namely, one aryl group and two aryloxy groups directly bonded to the boron atom. Two new optically active C_2 symmetric borepins, **19** and **20**, were thus synthesized (Figure 3).

Borepin **19** was prepared *in situ* by treating the bis(trimethylsilyl) ether of (*S*)-(−)-1,1′-bi-2-naphthol with dichlorophenylborane in dichloromethane from 0 °C to room temperature for 2 h. Borepin **19** precipitated from the solution during the course of the reaction. Treatment of the bis(trimethylsilyl) ether of (*S*)-(−)-3,3′-diphenyl-1,1′-bi(2-naphthol) (**21**) with dibromophenylborane in 1,2-dichloroethane at room temperature for 1 h gave the intermediate mono-binding compound **22** (eq 4). With heating at elevated temperature following the removal of trimethylsilyl bromide, the cyclization of **22** occurred to give **20**. Borepins **19** and **20** were too moisture-sensitive to permit their isolation in pure form. However, ^1H, ^{13}C, and ^{11}B NMR analysis clearly indicated the quantitative formation of **19** and **20** of high purity. As an alternative method for obtaining **20**, the use of dichlorophenylborane required a higher reaction temperature and longer reaction time for the cyclization of intermediate **23**,[18] and **20** was obtained as a relatively impure solid.

The enantioselective trifluoromethylation of the potassium enolate of propiophenone was carried out. The potassium enolate used was found to be the *Z*-isomer

(17) A review and recent papers: (a) Brown, H. C.; Jadhav, P. K.; Midland, M. M. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: Orlando, 1983; Vol. 2, pp 1–69. (b) Kaufmann, D.; Boese, R. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 545. (c) Takasu, M.; Yamamoto, H. *Synlett* **1990**, 194. (d) Sartor, D.; Saffrich, J.; Helmchen, G.; Richards, C. J.; Lambert, H. *Tetrahedron: Asymmetry* **1991**, *2*, 639. (e) Hattori, K.; Yamamoto, H. *J. Org. Chem.* **1992**, *57*, 3264. (f) Corey, E. J.; Loh, T.-P.; Roper, T. D.; Azimioara, M. D.; Noe, M. C. *J. Am. Chem. Soc.* **1992**, *114*, 8290. (g) Ishihara, K.; Mouri, M.; Gao, Q.; Maruyama, T.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 11490 and references cited therein.

(18) Intermediate **23** was isolated; its NMR data are as follows: ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (1 H, s), 7.96 (1 H, s), 7.95–7.72 (2 H, m), 7.67 (4 H, d, *J* = 7.4 Hz), 7.49–7.19 (15 H, m), 6.97–6.94 (2 H, m), −0.67 (9 H, s, $Si(CH_3)_3$); ^{11}B NMR (CH_2Cl_2) δ 38 (br). The structure of **22** was deduced by analogy with **23**.



21 22 : X = Br 23 : X = Cl (4)

almost exclusively (Z/E > 99/1).[19] The results of the enantioselective trifluoromethylation are shown in Table 5. Borepin **19** afforded 2-(trifluoromethyl)propiophenone in 12% ee yield. Bulky and almost pure borepin **20**, generated using dibromophenylborane, showed fair enantioselectivity (45% ee). With borepin **20** prepared by the dichlorophenylborane method, the same product was obtained in 42% ee yield (run 3). The better chemical yield by the latter borepin **20** is probably attributable to optically active contamination. Thus, the effective enantioselective trifluoromethylation required considerably bulky, optically active Lewis acids such as borepin **20**.

Conclusions

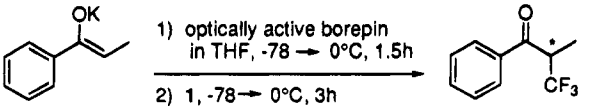
A new method for the trifluoromethylation of ketone enolates has been developed. By a judicious choice of boron Lewis acid and trifluoromethylating agent, controlled regio-, diastereo-, and enantioselective trifluoromethylation is possible. This methodology should prove of broad utility in the synthesis of trifluoromethylated organic compounds.

Experimental Section

General. Melting points were uncorrected. ^1H and ^{19}F NMR spectra were recorded with a 200 MHz NMR spectrometer, unless otherwise noted. ^{11}B and ^{13}C NMR spectra and NOESY spectra were obtained with a 500 MHz NMR spectrometer. ^{19}F NMR chemical shifts were reported in ppm downfield from CCl_3F as an internal reference. $BF_3{\cdot}Et_2O$ was used as an external reference for ^{11}B NMR and $CDCl_3$ as an internal reference for ^{13}C NMR. Mass spectra were recorded at 70 eV. The ee of 2-(trifluoromethyl)propiophenone was determined using a HPLC apparatus with two connected columns (4.6 mm ϕ × 250 mm × 2, particle size 5 μm) packed with Sumichiral OA-2000 (flow rate; 1 mL/min: eluent; hexane−$CF_2ClCFCl_2$−1,1,1,3,3,3-hexafluoro-2-propanol−trifluoroacetic acid, 800:40:0.2:0.04).

Materials. Trifluoromethylating agents **1**, **7**, **8**, and **9** and the perfluorooctylating agent **18** were prepared according to the reported methods.[10] 2-Mercaptobiphenyl, a starting material for **1** and **7**, was prepared on a large scale in high yield by conversion of sodium 2-phenylphenolate to *O*-(2-biphenylyl) dimethylthiocarbamate, followed by pyrolysis and hydrolysis.[21] Borole **4** was prepared by the reported method.[22,23] Reagents **1**, **8**, and **18** and borole **4** are commercially available from Daikin Chemical Sales, Ltd. (Japan). Dichlorophenylborane was distilled under reduced pressure before use. Dibromophenylborane,[24] 2-(*m*-nitrophenyl)-1,3,2-benzodioxaborole (**5**),[23] and mesityleneboronic acid[25] were prepared according to literature procedures. 2-Methyl-1-indanone was prepared in 84% yield by methylating the potassium enolate of 1-indanone (generated using KH) with methyl iodide in the presence of Et_3B.[13] Reaction solvents were dried by the usual methods before use. Other commercially available compounds were used without further purification, unless otherwise noted.

Table 5. Enantioselective Trifluoromethylation Using Optically Active Borepins 19 and 20



run[a]	borepin	yield(%)[b]	ee(%)[c]	remaining 1(%)[b]
1	**19**	31 (62)	12	50
2	**20**[d]	20 (54)	45	63
3	**20**[e]	41 (64)	42	36

[a] Potassium enolate of propiophenone was generated *in situ* by treatment of propiophenone with KH in THF at rt for 1 h. Mol ratios of propiophenone/KH/borepin/**1** were 1.2/1.2/1.25/1.0 for all runs. [b] Yields were determined by ^{19}F NMR relative to an internal standard (benzotrifluoride). Values are calculated based on **1** used and values in parentheses are based on consumed **1**. [c] Enantiomeric excesses were determined by HPLC analysis. Their optical rotation was (+) ($[\alpha]^{22}_D$ of 2-(trifluoromethyl)propiophenone obtained in 35% ee yield using borepin **20** was +3.6 (c = 1, $CHCl_3$)), but the absolute configuration was not determined. [d] Synthesized using dibromophenylborane (method A; see Experimental Section). [e] Synthesized using dichlorophenylborane (method B; see Experimental Section).

Preparation of 2-Mesityl-1,3,2-benzodioxaborole (14). A mixture of catechol (2.01 g, 18.3 mmol) and mesityleneboronic acid (3.00 g, 18.3 mmol) in toluene (60 mL) was heated under reflux for 12 h using a Dean−Stark device to remove water by azeotropy. Evaporation of toluene and addition of anhyd hexane (20 mL) yielded crystalline needles of **14** in 83% yield. **14**: mp 129.8−131.6 °C (hexane−toluene); ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 (2 H, dd, J = 5.8, 3.4 Hz), 7.15 (2 H, dd, J = 5.8, 3.4 Hz), 6.94 (2 H, s), 2.55 (6 H, s), 2.34 (3 H, s); ^{11}B NMR ($CDCl_3$) δ 32.9 (br); IR (KBr) 2969, 1610, 1469, 1432, 1306 cm^{-1}; MS m/z 238 (M^+), 223 ($M^+ - CH_3$). Anal. Found: C, 75.52; H, 6.32%. Calcd for $C_{15}H_{15}BO_2$: C, 75.67; H, 6.35%.

Preparation of 2-Mesitylphenanthro[9,10-*d*]-1,3,2-dioxaborole (15). Under an argon atm, $NaBH_4$ pellets (688 mg, 18.2 mmol) were added to a stirred solution of 9,10-phenanthrenequinone (2.54 g, 12.2 mmol) in anhyd DMF (24 mL) cooled in an ice bath.[26] After stirring for 2 h at rt, the reaction mixture was cooled in an ice bath and acetic acid (2.77 mL, 48.4 mmol) was added dropwise to the reaction mixture. After stirring for 30 min at rt, the reaction mixture was poured into water and extracted with toluene. Under an argon atm, the extract was washed with water and transferred to a flask containing mesityleneboronic acid (2.00 g, 12.2 mmol) equipped with a Dean−Stark device. Water and toluene used for the extraction were purged with argon gas before use in order to prevent the air oxidation of 9,10-phenanthrenediol. This mixture was heated under reflux for 16 h to remove water. Concentration of the reaction mixture followed by the addition of anhyd hexane gave 3.61 g (88%) of **15** as crystalline needles. **15**: mp 214.3−215.8 °C (hexane−toluene); ^1H NMR (500 MHz, $CDCl_3$) δ 8.76 (2 H, d, J = 8 Hz), 8.29 (2 H, dd, J = 8, 1 Hz),

(19) The potassium enolate of propiophenone generated under the same conditions was treated with chlorotrimethylsilane at −78 °C to rt to give the corresponding *Z*-isomeric enol trimethylsilyl ether[20] almost exclusively (Z/E > 99/1 by ^1H NMR).

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(26) Cho, H.; Harvey, R. G. *J. Chem. Soc., Perkin Trans. 1* **1976**, 836.

7.72 (2 H, t, J = 8 Hz), 7.66 (2 H, dt, J = 1, 8 Hz), 6.99 (2 H, s), 2.69 (6 H, s), 2.37 (3 H, s); ^{11}B NMR ($CDCl_3$) δ 33.1 (br); IR (KBr) 2965, 2920, 1656, 1607, 1432, 1368, 1337, 1309 cm^{-1}; MS m/z 338 (M^+), 323 ($M^+ - CH_3$). Anal. Found: C, 81.38; H, 5.66%. Calcd for $C_{23}H_{19}BO_2$: C, 81.68; H, 5.66%.

Preparation of (*S*)-4-Phenyldinaphtho[2,1-*d*:1′,2′-*f*]-[1,3,2]dioxaborepin (19). Under an argon atm, dichlorophenylborane (294 mg, 1.85 mmol) was added dropwise to a solution of the bis(trimethylsilyl)ether of (*S*)-(−)-1,1′-bi-2-naphthol (796 mg, 1.85 mmol) in anhyd dichloromethane (2.5 mL) cooled in an ice bath. After stirring for 2 h at rt, the solvent was evaporated under reduced pressure to obtain white solid **19**. Borepin **19** was so moisture-sensitive that it was used without further purification. **19**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (2 H, dm, J = 7 Hz), 7.95 (2 H, d, J = 8.8 Hz), 7.91 (2 H, d, J = 8 Hz), 7.60 (1 H, tm, J = 7 Hz), 7.54 (2 H, d, J = 8.8 Hz), 7.51 (2 H, t, J = 7 Hz), 7.42 (2 H, dt, J = 1, 8 Hz), 7.31 (2 H, d, J = 8 Hz), 7.24 (2 H, dt, J = 1, 8 Hz); ^{13}C NMR[27] ($CDCl_3$) δ 152.2, 135.8, 132.7, 132.6, 130.9, 130.1, 128.0, 127.9, 127.0, 125.9, 124.6, 121.3, 120.4; ^{11}B NMR ($CDCl_3$) δ 32.3 (br).

Preparation of (*S*)-4-Phenyl-{3,3′-diphenyldinaphtho-[2,1-*d*:1′,2′-*f*]}[1,3,2]dioxaborepin (20). Method A: Under an argon atm, dibromophenylborane (1.55 mL of 1.21 M solution in anhyd 1,2-dichloroethane, 1.88 mmol) was added dropwise to a solution of **21**[28] (1.09 g, 1.88 mmol) in anhyd 1,2-dichloroethane (4 mL) cooled in an ice bath. After stirring for 1 h at rt, the bath temperature was gradually raised to 105 °C for 1 h while the volatile components were distilled out. The resulting oil was cooled to 50 °C and dried under vacuum for 1 h at 50 °C to obtain **20** as a white amorphous solid.

Method B: Under an argon atm, dichlorophenylborane (294 mg, 1.85 mmol) was added to a solution of **21** (1.08 g, 1.85 mmol) in anhyd dichloromethane (1.5 mL) cooled in an ice bath. After stirring for 3 h at rt, the solvent was evaporated under reduced pressure to give crude **23**. Compound **23** was gradually heated from rt to 130 °C under reduced pressure. After heating for 13 h at 130 °C under vacuum, **20** was obtained as a white amorphous solid. **20**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (2 H, s), 7.97 (2 H, d, J = 8 Hz), 7.73 (4 H, dm, J = 8 Hz), 7.56–7.50 (6 H, m), 7.48 (2 H, dt, J = 1, 8 Hz), 7.40 (2 H, d, J = 8 Hz), 7.32–7.28 (3 H, m), 7.02 (2 H, t, J = 7 Hz), 6.98 (2 H, dm, J = 7 Hz); ^{13}C NMR[27] ($CDCl_3$) δ 149.7, 138.0, 136.4, 134.7, 132.5, 132.0, 130.6, 130.3, 130.2, 128.1, 128.0, 127.3, 127.2, 126.8, 125.9, 124.9, 121.4; ^{11}B NMR ($CDCl_3$) δ 34 (br).

Trifluoromethylation of Enolate Anions. A General Procedure. Under an argon atm, a ketone (1.2 mmol) was added dropwise to a suspension of KH (1.2 mmol) in anhyd THF (2 mL) cooled in an ice bath. After stirring for 1 h at rt, the reaction mixture was cooled to −78 °C using a dry ice–acetone bath, and then a boron compound (1.2 mmol) [a solution of borepin **19** or **20** (1.25 mmol) in anhyd THF (1.5 mL) for enantioselective trifluoromethylation] was added to the mixture. After stirring for 1 h at −78 °C, a trifluoromethylating agent (1.0 mmol) was added to the mixture and the mixture was gradually warmed to 0 °C in a period of 2.5 h. After benzotrifluoride (1.0 mmol) as an internal standard was added to the reaction mixture, the reaction mixture was analyzed by ^{19}F NMR. The results are shown in Tables 1–5. The reaction mixture was then poured into dilute hydrochloric acid and extracted with ether. The extract was washed with water and brine, dried with magnesium sulfate, and filtered. After evaporation of the solvent, the residue was column chromatographed on silica gel using a 20:1 mixture of hexane and ether as an eluent to isolate the products.

The structures of the products were determined by spectral and elemental analyses of the isolated products or comparison with authentic samples. The relative stereochemistry of the CF_3 groups in **11**, **12**, and **17** was determined by NOESY spectra; NOE's were observed between 18-CH_3 group and 16-H in **11α**, CH_3 group and 6-H in ***trans*-12**, 2-H and 6-H in ***cis*-12**, and CH_3 group and 8-H in **17α**. Data of new compounds are as follows.

2-(Trifluoromethyl)-1-indanone: mp 67.3–67.9 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 7.82 (1 H, dm, J = 7.5 Hz), 7.67 (1 H, dt, J = 1.2, 7.5 Hz), 7.51 (1 H, dm, J = 7.5 Hz), 7.44 (1 H, tm, J = 7.5 Hz), 3.51–3.20 (3 H, m); ^{19}F NMR (CD_3CN) −67.0 (d, J = 10.3 Hz); IR (KBr) 1724, 1602, 1345, 1250, 1184, 1168, 1100 cm^{-1}; MS m/z 200 (M^+), 131 ($M^+ - CF_3$). Anal. Found: C, 60.13; H, 3.54%. Calcd for $C_{10}H_7F_3O$: C, 60.01; H, 3.53%.

2,2-Bis(trifluoromethyl)-1-indanone: mp 91.4–93.4 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 7.88 (1 H, dm, J = 7.5 Hz), 7.74 (1 H, dt, J = 1, 7.5 Hz), 7.56 (1 H, dm, J = 7.5 Hz), 7.50 (1 H, tm, J = 7.5 Hz), 3.61 (2 H, s); ^{19}F NMR ($CDCl_3$) −69.3 (s); IR (KBr) 1765, 1730, 1600, 1278, 1219, 1182, 1016 cm^{-1}; MS m/z 268 (M^+), 199 ($M^+ - CF_3$). Anal. Found: C, 49.23; H, 2.28%. Calcd for $C_{11}H_6F_6O$: C, 49.27; H, 2.26%.

2-Methyl-2-(trifluoromethyl)-1-indanone: oil; ^{1}H NMR ($CDCl_3$) δ 7.82 (1 H, dm, J = 7.7 Hz), 7.67 (1 H, dt, J = 1, 7.7 Hz), 7.49 (1 H, dm, J = 7.7 Hz), 7.44 (1 H, tm, J = 7.7 Hz), 3.57 (1 H, d, J = 17.6 Hz), 3.03 (1 H, d, J = 17.6 Hz), 1.50 (3 H, s); ^{19}F NMR ($CDCl_3$) −74.1 (s); IR (neat) 1732, 1608, 1301, 1205, 1164, 1113 cm^{-1}; MS m/z 214 (M^+), 199 ($M^+ - CH_3$), 145 ($M^+ - CF_3$). Anal. Found: C, 61.55; H, 4.40%. Calcd for $C_{11}H_9F_3O$: C, 61.69; H, 4.24%.

3,3,3-Trifluoropropiophenone: wax; ^{1}H NMR ($CDCl_3$) δ 7.93 (2 H, dm, J = 7 Hz), 7.63 (1 H, tm, J = 7 Hz), 7.50 (2 H, tm, J = 7 Hz), 3.79 (2 H, q, J = 10 Hz); ^{19}F NMR ($CDCl_3$) −62.4 (t, J = 10 Hz); IR (KBr) 1687, 1598, 1377, 1284, 1229, 1132, 1100 cm^{-1}; MS m/z 188 (M^+), 105 ($PhCO^+$). Anal. Found: C, 57.23; H, 3.67%. Calcd for $C_9H_7F_3O$: C, 57.45; H, 3.75%.

2-(Trifluoromethyl)propiophenone: oil; ^{1}H NMR ($CDCl_3$) δ 7.95 (2 H, dm, J = 7 Hz), 7.64 (1 H, tm, J = 7 Hz), 7.51 (2 H, tm, J = 7 Hz), 4.25 (1 H, dd, J = 7, 8 Hz), 1.48 (3 H, d, J = 7 Hz); ^{19}F NMR ($CDCl_3$) −68.7 (d, J = 8 Hz); IR (neat) 1694, 1598, 1334, 1273, 1224, 1171, 1134 cm^{-1}; MS m/z 202 (M^+), 182 ($M^+ - HF$), 105 ($PhCO^+$). Anal. Found: C, 59.49; H, 4.53%. Calcd for $C_{10}H_9F_3O$: C, 59.41; H, 4.49%.

(16*R*)-(Trifluoromethyl)estrone 3-methyl ether (11α): mp 167.2–168.9 °C (ethyl acetate–hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (1 H, d, J = 8.6 Hz), 6.73 (1 H, dd, J = 8.6, 2.8 Hz), 6.65 (1 H, d, J = 2.8 Hz), 3.78 (3 H, s), 3.25 (1 H, ddq, J = 2.2, 11, 11 Hz), 2.91 (2 H, m), 2.41 (1 H, m), 2.30–2.26 (2 H, m), 2.02–1.94 (3 H, m), 1.68 (1 H, m), 1.60–1.43 (4 H, m), 0.97 (3 H, s); ^{19}F NMR ($CDCl_3$) −66.59 (d, J = 11.1 Hz); IR (KBr) 2946, 1750, 1612, 1363, 1258, 1191, 1116 cm^{-1}; MS m/z 352 (M^+), 337 ($M^+ - CH_3$), 282 ($M^+ - CF_3H$), 267 ($M^+ - CF_3H$, CH_3). Anal. Found: C, 68.09; H, 6.70%. Calcd for $C_{20}H_{23}F_3O_2$: C, 68.17; H, 6.58%.

(16*S*)-(Trifluoromethyl)estrone 3-methyl ether (11β): mp 184.5–186.2 °C (ethyl acetate–hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (1 H, d, J = 8.4 Hz), 6.73 (1 H, dd, J = 8.4, 2.8 Hz), 6.65 (1 H, d, J = 2.8 Hz), 3.78 (3 H, s), 2.97–2.87 (3 H, m), 2.45–2.35 (2 H, m), 2.30 (1 H, m), 2.05–2.00 (2 H, m), 1.85 (1 H, dt, J = 10.8, 12.8 Hz), 1.67–1.43 (5 H, m), 0.97 (3 H, s); ^{19}F NMR ($CDCl_3$) −66.61 (d, J = 10.3 Hz); IR (KBr) 2940, 1755, 1612, 1354, 1253, 1158, 1106 cm^{-1}; MS m/z 352 (M^+), 332 ($M^+ - HF$), 267 ($M^+ - CF_3H$, CH_3). Anal. Found: C, 68.29; H, 6.71%. Calcd for $C_{20}H_{23}F_3O_2$: C, 68.17; H, 6.58%.

Ethyl 2-(trifluoromethyl)phenylacetate: oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.41 (2 H, m), 7.40–7.26 (3 H, m), 4.30 (1 H, q, J = 8.6 Hz), 4.26 (1 H, dq, J = 10.8, 7.1 Hz), 4.20 (1 H, dq, J = 10.8, 7.1 Hz), 1.26 (3 H, t, J = 7.1 Hz); ^{19}F NMR ($CDCl_3$) −68.2 (d, J = 8.6 Hz); IR (neat) 1748, 1350, 1259, 1220, 1155, 1110 cm^{-1}; MS m/z 232 (M^+), 187 ($M^+ - EtO$), 159 ($M^+ - CO_2Et$). Anal. Found: C, 56.60; H, 4.68%. Calcd for $C_{11}H_{11}F_3O_2$: C, 56.90; H, 4.78%.

***cis*-2-Methyl-6-(trifluoromethyl)cyclohexanone (*cis*-12)**: oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.07 (1 H, m), 2.45–2.35 (2 H, m), 2.15 (1 H, m), 1.98 (1 H, m), 1.84–1.71 (2 H, m), 1.45 (1 H, m), 1.06 (3 H, d, J = 6.5 Hz); ^{19}F NMR ($CDCl_3$) −69.6 (d, J = 7.9 Hz); IR (neat) 2940, 2872, 1730, 1331, 1272, 1170, 1145, 1098 cm^{-1}; MS m/z 180 (M^+), 165 ($M^+ - CH_3$).

(27) The ^{13}C NMR spectra of borepins **19** and **20** did not exhibit peaks due to the carbons directly bonded to the boron atoms. Under the same measurement conditions, the ^{13}C NMR spectrum of the known borole **4** did not show the peak of the carbon directly bonded to the boron atom.

(28) Chapuis, C.; Jurczak, J. *Helv. Chim. Acta* **1987**, *70*, 436.

Anal. Found: C, 53.61; H, 6.34%. Calcd for $C_8H_{11}F_3O$: C, 53.33; H, 6.15%.

***trans*-2-Methyl-6-(trifluoromethyl)cyclohexanone (*trans*-12)**: oil; ^1H NMR (500 MHz, $CDCl_3$) δ 3.15 (1 H, qt, J = 9.9, 5.9 Hz), 2.65 (1 H, m), 2.15 (1 H, m), 2.10–2.00 (2 H, m), 1.92 (1 H, m), 1.78 (1 H, m), 1.55 (1 H, m), 1.12 (3 H, d, J = 6.7 Hz); ^{19}F NMR ($CDCl_3$) −66.6 (d, J = 9.9 Hz); IR (neat) 2944, 2878, 1722, 1332, 1274, 1242, 1194, 1141 cm^{-1}; MS *m/z* 180 (M^+), 165 ($M^+ - CH_3$); HRMS calcd for $C_8H_{11}F_3O$ 180.07620, found 180.07640.

2-Methyl-2-(trifluoromethyl)cyclohexanone (13): oil; ^1H NMR (500 MHz, $CDCl_3$) δ 2.55–2.40 (2 H, m), 2.14 (1 H, m), 1.96–1.72 (5 H, m), 1.36 (3 H, s); ^{19}F NMR ($CDCl_3$) −73.6 (s); IR (neat) 2947, 2874, 1732, 1272, 1194, 1170, 1135 cm^{-1}; MS *m/z* 180 (M^+), 165 ($M^+ - CH_3$); HRMS calcd for $C_8H_{11}F_3O$ 180.07620, found 180.07652.

Perfluorooctylation of an Enolate Anion. Under similar conditions to those outlined above using **1**, perfluorooctylation of the potassium enolate generated from cyclohexanone (66 mg, 0.68 mmol) and KH (27 mg, 0.68 mmol) was conducted by using perfluorooctylating agent **18** (423 mg, 0.56 mmol) and borole **4** (132 mg, 0.68 mmol). The ^{19}F NMR analysis using benzotrifluoride as an internal standard showed that 2-(perfluorooctyl)cyclohexanone was produced in 71% yield. 2-(Perfluorooctylidene)cyclohexanone was not detected in this reaction mixture. However, 2-(perfluorooctyl)cyclohexanone underwent partial dehydrofluorination when chromatographed on silica gel for purification. Thus, the resulting 1:2.5 mixture (173 mg, 0.34 mmol) of 2-(perfluorooctyl)cyclohexanone and 2-(perfluorooctylidene)cyclohexanone was treated with triethylamine (42 mg, 0.41 mmol) in dichloromethane (2 mL) at rt for 2 h. After evaporation of the solvent, the residue was column chromatographed on silica gel to give pure 2-(perfluorooctylidene)cyclohexanone in overall 60% yield from cyclohexanone.

2-(Perfluorooctylidene)cyclohexanone: wax; ^1H NMR ($CDCl_3$) δ 2.66 (2 H, m), 2.58 (2 H, t, J = 7 Hz), 2.03–1.80 (4 H, m); ^{19}F NMR ($CDCl_3$) −81.0 (3 F, t, J = 9.8 Hz), −114.1 (2 F, m), −120.7 (1 F, br s), −122.1 (4 F, m), −122.9 (2 F, m), −123.6 (2 F, m), −126.3 (2 F, m); IR (neat) 2952, 1715, 1202, 1148 cm^{-1}; FAB-MS, positive *m/z* 497 $(M + H)^+$. Anal. Found: C, 34.17; H, 1.62%. Calcd for $C_{14}H_8F_{16}O$: C, 33.89; H, 1.63%.