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Lewis Acid Catalysis in Supercritical Carbon Dioxide. Use of Poly(ethylene glycol) Derivatives and Perfluoroalkylbenzenes as Surfactant Molecules Which Enable Efficient Catalysis in $ScCO_2$

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Lewis acid catalysis in supercritical carbon dioxide (CO_2) was investigated. While solubility of most organic materials is low in $scCO_2$, poly(ethylene glycol) derivatives or perfluoroalkylbenzenes were found to work as surfactants to dissolve organic materials in $scCO_2$. In the presence of these molecules, Lewis acid catalyzed organic reactions such as aldol-, Mannich-, and Friedel−Crafts-type reactions proceeded smoothly in $scCO_2$. Formation of emulsions was observed in these reactions, and the systems were studied in detail.

Introduction

Supercritical fluids (SCF) are an attractive alternative to conventional solvents and are becoming more important in organic chemistry and related industries.[1] In particular, supercritical carbon dioxide ($scCO_2$) is currently well investigated as an environmentally friendly solvent and is widely used due to its low cost, nontoxicity and nonflammability, ease of recovery and reuse, and moderate critical conditions ($T_c = 31.1$ °C, $P_c = 7.4$ MPa), etc. On the other hand, a drawback is that CO_2 behaves like a hydrocarbon solvent and that reactants and/or catalysts have often only low solubility in CO_2. Addition of small quantities of co-solvents was attempted in part to improve the solubility in $scCO_2$. Introduction of perfluorinated side chains in reactants and/or ligands was also investigated to increase the solubility in $scCO_2$.[2] Alternatively, dispersion systems such as water−SCF biphasic media with several kinds of surfactants were investigated in organic synthesis including hydrogenation reactions. For example, Tumus and co-workers studied hydrogenation reactions of alkenes in a water−CO_2 biphasic system, which formed microemulsions with ionic perfluoropolyether ammonium carboxylate (PEPE CO_2^--NH_4^+).[3] Jessop and co-workers used tetraalkylammonium sulfate as a surfactant in hydrogenation reactions of arenes in water−supercritical ethane.[4] In polymer synthesis, successful dispersion polymerization reactions of methyl methacrylate and others in CO_2 with fluorinated polymer surfactants were reported by DeSimone et al.[5] Hay et al. used polysiloxane instead of fluorinated polymers in poly(methyl methacrylate) synthesis.[6] However, these reaction systems have not been applied to other organic reactions, and more simple reaction systems are desired to dissolve many reactants or catalysts and, thus, to accelerate the reactions in $scCO_2$.

On the other hand, we have recently developed several Lewis acid catalyzed organic reactions in water. In these reactions, surfactant molecules which create colloidal particles with organic compounds accelerated the reactions by concentrating substrates and catalysts inside the particles.[7] For example, scandium triflate catalyzed aldol reactions of aldehydes with silicon enolates proceeded smoothly in water with sodium dodecyl sulfate (SDS) as a surfactant. In this reaction, emulsions were formed in water, and the reactions proceeded faster in water than in organic solvents.[7c]

Bearing these experimental results in mind, we thought that some specific molecules might work as surfactants and accelerate organic reactions in $scCO_2$ by forming concentrated colloidal dispersions. We now report that poly(ethylene glycol) (PEG) derivatives or 1-dodecyloxyl-4-perfluoroalkylbenzenes work as surfactants in several organic reactions such as aldol-, Mannich-, and Friedel−Crafts-type reactions in $scCO_2$.[8] Formation of emulsions was observed in these $scCO_2$/surfactant systems. The use

(1) See, for example: (a) Noyori, R., Ed. Supercritical Fluids. In *Chem. Rev.* **1999**, *99*, 353−634. (b) Symposium on supercritical fluids in *Ind. Eng. Chem. Res.* **2000**, *39*, 4441−4907.

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(7) See, for example: (a) Kobayashi, S.; Wakabayashi, T.; Nagayama, S.; Oyamada, H. *Tetrahedron Lett.* **1997**, *38*, 4559. (b) Kobayashi, S.; Mori, Y.; Nagayama, S.; Manabe, K. *Green Chem.* **1999**, 175. (c) Manabe, K.; Mori, Y.; Wakabayashi, T.; Nagayama, S.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 7202. (d) Manabe, K.; Aoyama, N.; Kobayashi, S. *Adv. Synth. Catal.* **2001**, *343*, 174. (e) Manabe, K.; Mori, Y.; Kobayashi, S. *Tetrahedron* **2001**, *57*, 2537.

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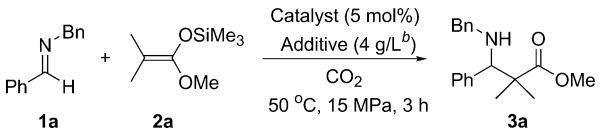
TABLE 1. Effects of Catalysts and Additives in $ScCO_2$



1a **2a** **3a**

entry	catalyst	additive	yield (%)
1	$Yb(OTf)_3$	none	10
2	$Yb(OTf)_3$	PEG[a]	72
3	$Yb(OTf)_3$	CH_2Cl_2	36
4	$Yb(OTf)_3$	CH_3CN	35
5	$Yb(OTf)_3$	CH_2Cl_2[c]	58
6	$Yb(OTf)_3$	hexane[d]	26
7	$Yb(OSO_2C_4F_9)_3$	none	47
8	$Yb(OSO_2C_8F_{17})_3$	none	62
9	$Yb(OSO_2C_4F_9)_3$	PEG[a]	64
10	$Yb(OSO_2C_8F_{17})_3$	PEG[a]	40

[a] Poly(ethylene glycol) (average molecular weight was 400). [b] Additive (ca. 40 mg) was added in a 10 mL reaction vessel. [c] Reaction was carried out in CH_2Cl_2. [d] Reaction was carried out in hexane.

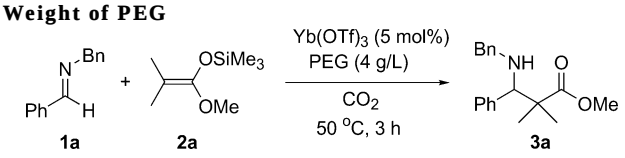
of surfactants to facilitate the formation of emulsions in a single $scCO_2$ phase is a novel approach to synthesize small organic molecules.

Results and Discussion

Ln(OTf)$_3$-Catalyzed Aldol- and Mannich-Type Reactions in the CO_2−PEG Derivative System. Aldol and Mannich reactions provide useful methods for construction of carbon−carbon bonds. Among them, Lewis acid mediated aldol reactions of silicon enolates with aldehydes and Mannich-type reactions of silicon enolates with imines (Mukaiyama-type reactions) have several advantages over conventional methods.[9]

In an initial trial, $Yb(OTf)_3$-catalyzed Mannich-type reaction[10] of imine **1a** with silicon enolate **2a** was conducted in $scCO_2$. The reaction proceeded very slowly, and the desired product was obtained in only 10% yield after 3 h. It was assumed that the low solubility of **1a** and **2a** in $scCO_2$ caused the low yield. We then tested several compounds which might work as surfactants to dissolve the substrates in $scCO_2$. While normal organic solvents such as dichloromethane or acetonitrile slightly improved the yield, poly(ethylene glycol) (PEG) was found to be much more effective (Table 1).[11] We also confirmed that in the absence of PEG the longer the perfluoroalkyl chains of ytterbium catalysts were, the higher the yields of the desired products (Table 1, entries 1, 7, and 8).[12] On the other hand, a reverse tendency was observed in the PEG−CO_2 system. The yield of the product in the $Yb(OTf)_3$−PEG system was higher than that in the $Yb(OSO_2C_4F_9)_3$−PEG or $Yb(OSO_2C_8F_{17})_3$−PEG system (Table 1, entries 2, 9, and 10). The formation of emulsions was observed in the presence of PEG (Figure 1, right), while substrates attached to the wall of the reaction vessel and did not spread out during the reaction without the additive (Figure 1, left). These facts indicated that PEG acted as a surfactant in $scCO_2$ and that the catalyst and substrates would be packed into the emulsion, and therefore, the reaction proceeded rapidly. The effect of pressure of CO_2 and average molecular weight (M_w) of PEG on the yield of the product is summarized in Table 2. The highest yield was obtained at 15 MPa using PEG of M_w = 400. This system was applicable to various substrates including imines derived from aromatic and heterocyclic as well as aliphatic aldehydes and silicon enolates derived from esters, thioesters, and a ketone (Table 3).

TABLE 2. Effect of Pressure of CO_2 and Molecular Weight of PEG



1a **2a** **3a**

entry	pressure (MPa)[a]	M_w[b]	yield (%)
1	10	400	39
2	15	400	72
3	20	400	46
4	25	400	39
5	15	200	39
6	15	600	52
7	15	1000	20

[a] Pressure of CO_2. [b] Molecular weight of PEG. PEG (ca. 40 mg) was added in a 10 mL reaction vessel.

We also found that the CO_2−PEG system was effective for scandium-catalyzed aldol reactions.[13] Interestingly, in this reaction, poly(ethylene glycol) dimethyl ether ($PEG(OMe)_2$, M_w = 500) was more effective than PEG. The effects of pressure of CO_2 and concentration of $PEG(OMe)_2$ on yields were examined, and the results are summarized in Chart 1. From these results, it was shown that lower pressure was better for the aldol reaction to obtain high yields in comparison to the Mannich-type reaction. Although the precise mechanism is not clear, a certain extent of CO_2 pressure might be necessary in the case of Mannich-type reactions to regenerate the catalyst from the catalyst−product complex at the surface or the inside of the particles.[14] On the other hand, in the correlation of the yields of the aldol adduct with the concentration of the additive, high yields of the aldol adduct were obtained at concentrations from 1 to 8 g/L, while the yield decreased at the concentration of 0.5 g/L. We also observed that the CO_2−$PEG(OMe)_2$ medium formed emulsions when the concentration of the additive was 1 g/L. The reaction state was a little cloudy in the

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(11) An example using PEG as a phase-transfer catalyst between a $scCO_2$ phase and a solid KCl salt phase in the cyanation reaction of benzyl chloride was reported: Chandler, K.; Culp, C. W.; Lamb, D. R.; Liotta, C. L.; Eckert, C. A. *Ind. Eng. Chem. Res.* **1998**, *37*, 3252.

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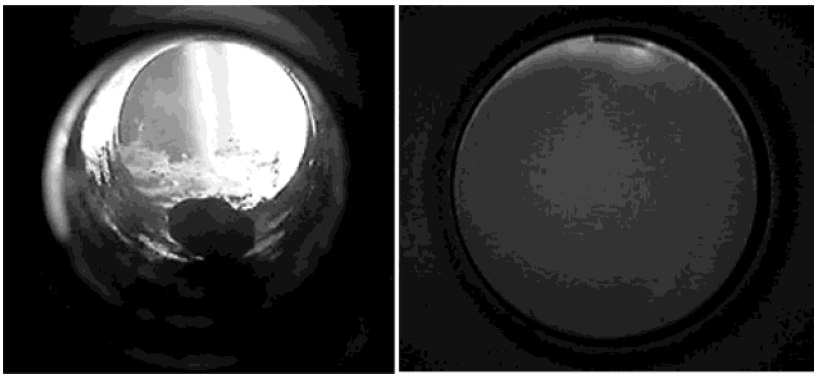
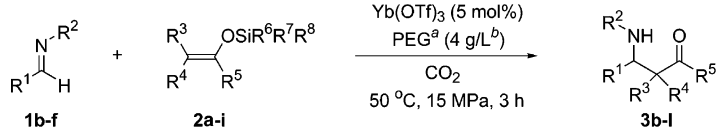


FIGURE 1. Reaction vessels of the $Yb(OTf)_3$-catalyzed Mannich reaction of imine **1a** with silicon enolate **2a** in CO_2: no additive (left); PEG added (right). The black lump is a stirring bar.

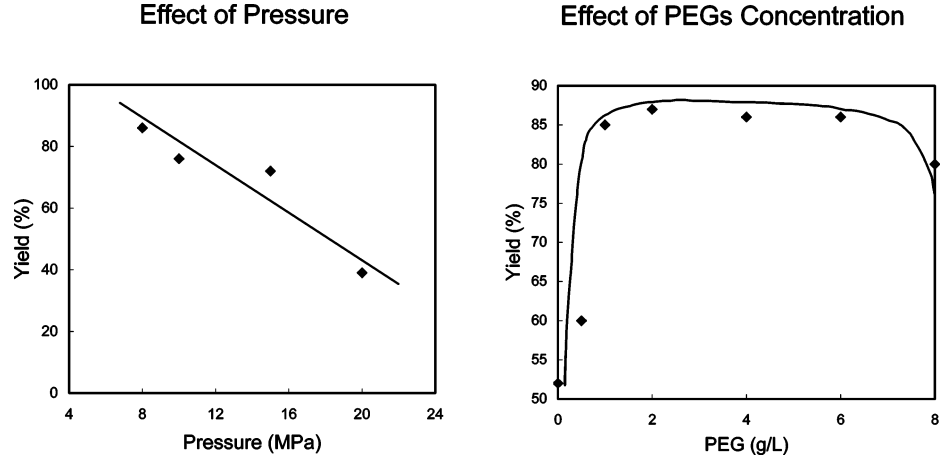
TABLE 3. Mannich-Type Reactions in the CO_2−PEG System



entry	R^1	R^2	imine	R^3	R^4	R^5	$SiR^6R^7R^8$	enolate	product	yield (%)	syn/anti
1	Ph	Ph	**1b**	Me	Me	OMe	$SiMe_3$	**2a**	**3b**	85	
2	Ph	Ph	**1b**	Me	Me	OMe	Si^tBuMe_2	**2b**	**3b**	97	
3	PhCH=CH−	Ph	**1c**	Me	Me	OMe	Si^tBuMe_2	**2b**	**3c**	74	
4	2-furyl	Ph	**1d**	Me	Me	OMe	$SiMe_3$	**2a**	**3d**	75	
5	Ph	*o*-$MeOC_6H_4$	**1e**	H	H	SEt	$SiMe_3$	**2c**	**3e**	91	
6	Ph	*o*-$MeOC_6H_4$	**1e**	H	Me	SEt	$SiMe_3$	**2d**[d]	**3f**	95	57/43
7	Ph	*o*-$MeOC_6H_4$	**1e**	Me	Me	SEt	$SiMe_3$	**2e**	**3g**	39	
8	Ph	*o*-$MeOC_6H_4$	**1e**	H	Me	OMe	Si^tBuMe_2	**2f**[e]	**3h**	68	38/62
9	Ph	*o*-$MeOC_6H_4$	**1e**	Me	H	OMe	Si^tBuMe_2	**2g**[f]	**3h**	63	31/69
10	cyclohexyl	Ph	**1f**	H	H	SEt	$SiMe_3$	**2c**	**3i**	89	
11	cyclohexyl	Ph	**1f**	H	H	OEt	Si^tBuMe_2	**2h**	**3j**	67	
12	cyclohexyl	Ph	**1f**	Me	Me	OMe	Si^tBuMe_2	**2b**	**3k**	44	
13[c]	Ph	Ph	**1b**	H	H	Ph	$SiMe_3$	**2i**[g]	**3l**	78[h]	

[a] Poly(ethylene glycol) (average molecular weight was 400). [b] PEG (ca. 40 mg) was added in a 10 mL reaction vessel. [c] The reaction was carried out at 8 MPa. [d] *E*/*Z* = 3/97. [e] *E*/*Z* = 87/13. [f] *E*/*Z* = 7/93. [g] 1.5 equiv was used. [h] The yield was determined by ^1H NMR analysis.

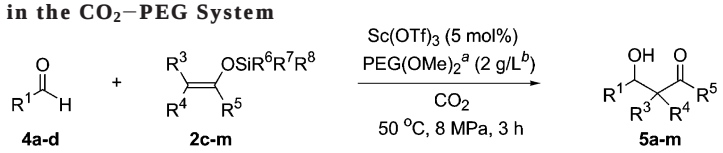
CHART 1. Effects of Pressure of CO_2 and Concentration of $PEG(OMe)_2$ in the Aldol Reaction of Aldehyde 4a with Silicon Enolate 2i at 50 °C for 3 h in the CO_2−$PEG(OMe)_2$ System (Conditions: 2 g/L (Left); 8 MPa (Right))



case of 0.5 g/L. It seemed that the critical micelle concentration (cmc) of this reaction system was between 0.5 and 1 g/L. We examined several examples of the aldol reactions in the CO_2−$PEG(OMe)_2$ system (Table 4). Not only benzaldehyde but also substituted aromatics, aliphatic, and α,β-unsaturated aldehydes reacted smoothly, and various silicon enolates derived from a ketone, esters, and thioesters also reacted well to afford the corresponding aldol adducts in high yields.

Aldol and Friedel−Crafts Reactions in $scCO_2$ Using 1-Dodecyloxy-4-perfluoroalkylbenzenes as Surfactants. PEG derivatives were found to work well as surfactants for the reactions in $scCO_2$. We then continued to search for more efficiently tuned molecules

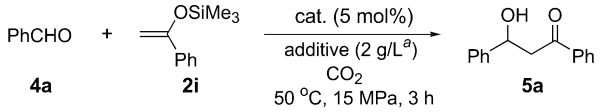
TABLE 4. Aldol Reactions in the CO_2−PEG System

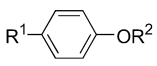


entry	R^1	aldehyde	R^3	R^4	R^5	$SiR^6R^7R^8$	enolate	product	yield (%)	syn/anti
1[c−e]	Ph	**4a**	H	H	Ph	$SiMe_3$	**2i**	**5a**	38	
2[c,e]	Ph	**4a**	H	H	Ph	$SiMe_3$	**2i**	**5a**	72 (52[n])	
3	*p*-ClC_6H_4	**4b**	H	H	Ph	$SiMe_3$	**2i**	**5b**	93	
4	*p*-MeC_6H_4	**4c**	H	H	Ph	$SiMe_3$	**2i**	**5c**	89	
5	Ph	**4a**	H	H	OEt	Si^tBuMe_2	**2h**[f]	**5d**	90	
6	PhCH=CH−	**4d**	H	H	OEt	Si^tBuMe_2	**2h**[d]	**5e**	89	
7	$PhCH_2CH_2$−	**4e**	H	H	OEt	Si^tBuMe_2	**2h**[f]	**5f**	78	
8	Ph	**4a**	H	Me	OMe	Si^tBuMe_2	**2f**[f,g]	**5g**	82	33/67
9	Ph	**4a**	Me	H	OMe	Si^tBuMe_2	**2g**[f,h]	**5g**	91	31/69
10	Ph	**4a**	H	H	SEt	$SiMe_3$	**2c**	**5h**	84	
11	Ph	**4a**	H	Me	SEt	$SiMe_3$	**2d**[i]	**5i**	91	26/74
12	Ph	**4a**	Me	Me	SEt	$SiMe_3$	**2e**	**5j**	51	
13	Ph	**4a**	H	Me	O^{t}Bu	$SiMe_3$	**2j**[j]	**5k**	48	29/71
14	Ph	**4a**	H	Me	O^{i}Pr	Si^tBuMe_2	**2k**[k]	**5l**	77	45/55
15	Ph	**4a**	Me	H	O^{i}Pr	Si^tBuMe_2	**2l**[l]	**5l**	96	37/63
16	Ph	**4a**	H	Me	OPh	Si^tBuMe_2	**2m**[m]	**5m**	62	34/66

[a] Poly(ethylene glycol) dimethyl ether (average molecular weight was 500). [b] $PEG(OMe)_2$ (ca. 20 mg) was added in a 10 mL reaction vessel. [c] The reaction was carried out at 15 MPa. [d] Poly(ethylene glycol) (average molecular weight was 400) was added. [e] Additive (4 g/L). [f] 1.5 equiv was used. [g] *E*/*Z* = 87/13. [h] *E*/*Z* = 7/93. [i] *E*/*Z* = 3/93. [j] *E*/*Z* = 96/4. [k] *E*/*Z* = 88/12. [l] *E*/*Z* = 12/88. [m] *E*/*Z* = 96/4. [n] Without $PEG(OMe)_2$.

TABLE 5. Effect of Additives and Catalysts





6a: R^1=C_8F_{17}, R^2=$C_{12}H_{25}$
6b: R^1=C_4F_9, R^2=$C_{12}H_{25}$
6c: R^1= H, R^2=$C_{12}H_{25}$
6d: R^1=C_8F_{17}, R^2=C_6H_{13}
6e: R^1=C_8F_{17}, R^2=CH_3

entry	cat.	additive	yield (%)
1	$Sc(OTf)_3$	**6a**	80
2	$Sc(OTf)_3$	**6b**	61
3	$Sc(OTf)_3$	**6c**	48
4	$Sc(OTf)_3$	**6d**	75
5	$Sc(OTf)_3$	**6e**	69
6	$Sc(OSO_2C_4F_9)_3$	**6a**	73
7	$Sc(OSO_2C_8F_{17})_3$	**6a**	51

[a] Additive (ca. 20 mg) was added in a 10 mL reaction vessel.

which act as surfactants in $scCO_2$. We designed a fluorosurfactant as an alternative and fixed a perfluoroalkyl chain as a CO_2-philic domain and an alkyl chain as a lipophilic domain. Based on this consideration, we prepared 1-dodecyloxy-4-heptadecafluorooctylbenzene (**6a**), which was tested in the $Sc(OTf)_3$-catalyzed aldol reaction of 1-trimethylsiloxy-1-phenylethene **2i** with benzaldehyde **4a** in $scCO_2$. It was found that the reaction proceeded smoothly in the presence of a small amount of **6a** to afford the corresponding aldol adduct in 80% yield (Table 5, entry 1). It should be noted that the yield was better than that obtained using $PEG(OMe)_2$ as an additive (Table 4, entry 2). In this system, we observed a tendency similar to that in the CO_2−PEG system regarding yields of the aldol reaction in that the longer the perfluoroalkylsulfonyl chains of the scandium catalysts were, the lower the yields of the desired product. In regard to the length of the perfluoroalkyl chains of the additives, interesting results were observed in the CO_2−fluorosurfactant systems. Namely, lower yields of the product were obtained when additive **6b** with a shorter perfluoroalkyl chain **6b** and one without a perfluoroalkyl chain (**6c**) were used. Also, the alkyl chain of the ether part effected the yields of the product. The longer the alkyl chain, the higher the yields of the aldol adduct were (Table 5, entries 4 and 5). While the formation of emulsions such as in the CO_2−PEG system was observed using **6a** (Figure 2, right), no emulsions were observed without the additive (Figure 2, left). When additive **6c** was used, the reaction mixture became slightly cloudy. These observations indicated that perfluoroalkylbenzenes acted as surfactants and that both the perfluoroalkyl and the alkyl chains of the ether domains were necessary to form the emulsions.

Several examples of the $Sc(OTf)_3$-catalyzed aldol type reactions of aldehydes with silicon enolates and $Yb(OTf)_3$-catalyzed Mannich-type reactions of imines with silicon enolates in the presence of **6a** in $scCO_2$ are shown in Tables 6 and 7, respectively. It is noted in most cases that the yields using **6a** are better than those using PEGs as an additive in $scCO_2$. Fluorosurfactant **6a** was recovered quantitatively from the reaction mixture by simple extraction with a fluorous solvent (FC-72), and the Lewis acid catalyst was also recovered and reused without loss of activity (see the Experimental Section).

The CO_2−fluorosurfactant system was successfully applied to other organic reactions. We found that fluorosurfactant **6a** was also effective for Friedel−Crafts alkylation and acylation reactions. We tested Friedel−Crafts alkylation of indoles, and several examples are shown in Table 8.[7d,15] This system gave alkylated indoles in higher yields than the system without the fluoro-

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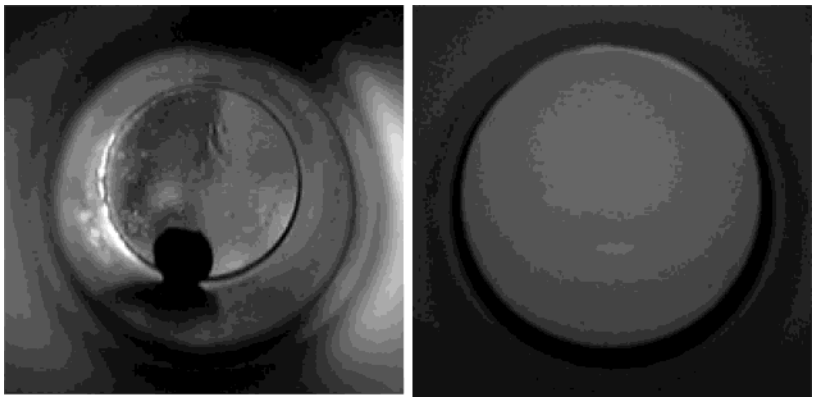
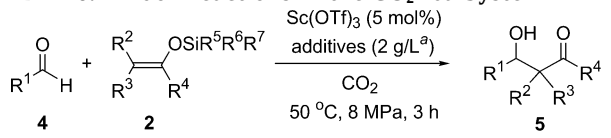


FIGURE 2. Reaction vessels of the $Sc(OTf)_3$-catalyzed aldol reaction of aldehyde **4a** with silicon enolate **2i** in CO_2: **6a** added (right); no additive (left). The black lump is a stirring bar.

TABLE 6. Aldol Reactions in the CO_2−6a System

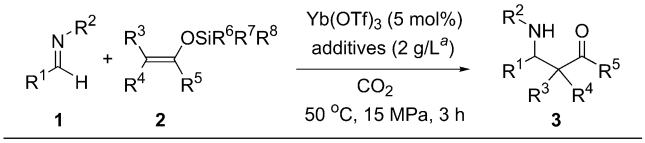


4 2 5

				yield (syn/anti)	
entry	aldehyde	enolate	product	**6a**	PEG(OMe)$_2$
1	**4a**	**2h**	**5d**	90 (−)	90 (−)
2	**4a**	**2c**[b]	**5h**	87 (−)	84 (−)
3	**4a**	**2f**[c]	**5g**	97 (40/60)	82 (33/67)
4	**4a**	**2g**[d]	**5g**	98 (50/50)	91 (31/69)
5	**4d**	**2h**	**5e**	99 (−)	89 (−)
6	**4e**	**2h**	**5f**	92 (−)	78 (−)

[a] Additive (ca. 20 mg) was added in a 10 mL reaction vessel. [b] 1.2 equiv was used. [c] E/Z = 87/13. [d] E/Z = 7/93.

TABLE 7. Mannich-Type Reactions in the CO_2−6a System



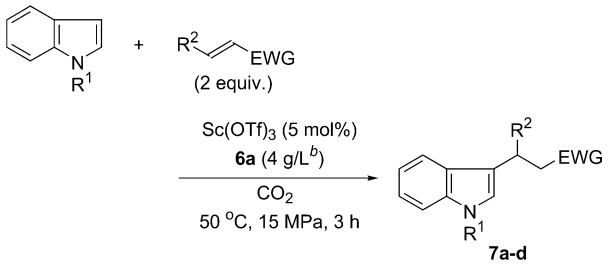
1 2 3

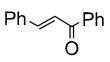
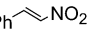
				yield (syn/anti)	
entry	imine	enolate	product	**6a**	PEG
1	**1b**	**2a**	**3b**	97 (−)	85[f] (−)
2[b]	**1b**	**2i**[c]	**3l**	61 (−)	78 (−)
3	**1e**	**2f**[d]	**3h**	82 (31/69)	68[f] (38/62)
4	**1e**	**2g**[e]	**3h**	73 (−)	63[f] (−)
5	**1f**	**2c**	**3i**	90 (−)	89[f] (−)

[a] Additive (ca. 20 mg) was added in a 10 mL reaction vessel. [b] Reaction was carried out at 8 MPa. [c] 1.5 equiv was used. [d] E/Z = 87/13. [e] E/Z = 7/93. [f] PEG (ca. 40 mg) was added in a 10 mL reaction vessel.

surfactant or with PEGs. We also confirmed the formation of emulsions in these reactions. We conducted further examinations of Friedel−Crafts acylation, and the results are summarized in Table 9. Not only acetylation but also benzoylation products were obtained in good yields. Moreover, an acid anhydride as well as acyl chlorides also worked well to give the corresponding aromatic ketones. In conventional methods, Friedel−Crafts acylation has been carried out in halogenated solvents (e.g., dichloromethane, dichloroethane) with a stoichiometric amount of a Lewis acid (e.g., $AlCl_3$, $FeCl_3$, $SnCl_4$).[16] Several metal triflates have been used to

TABLE 8. Friedel−Crafts Alkylation of Indol Derivatives in the CO_2−6a System



Entry	R^1	alkylating reagent	product	Yield (%)[a]
1	H		**7a**	69 (58)
2	H		**7b**	92 (74)
3	Me		**7c**	77 (59)
4	Me		**7d**	84 (71)

[a] Product yields without the additive are shown in parentheses. [b] **6a** (ca. 40 mg) was added in a 10 mL reaction vessel.

perform Friedel−Crafts acylation by catalytic quantities, but in halogenated solvents, acetonitrile, or nitromethane.[17] It is noted that Friedel−Crafts acylation proceeded smoothly in nonpolar $scCO_2$.

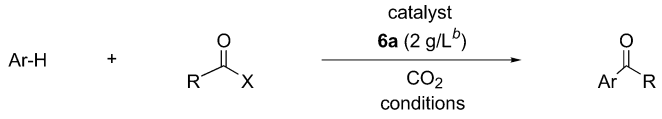
Conclusion

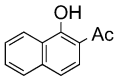
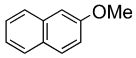
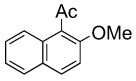
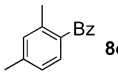
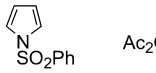
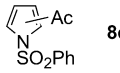
We have developed unique new media, $scCO_2$−surfactant systems. Among several molecules tested, poly(ethylene glycol) derivatives and perfluoroalkylbenzenes were found to work as efficient surfactant molecules in $scCO_2$. In these media, reactants and catalysts were homogenized to form emulsions, and Lewis acid-catalyzed fundamental carbon−carbon bond-forming reactions such as aldol, Mannich, and Friedel−Crafts alkylation and acylation reactions proceeded smoothly. The length of the

(16) (a) *Friedel−Crafts and Related Reactions*; Olah, G. A., Ed.; New York, 1963−64; Vols. I−IV. (b) Olah, G. A. *Friedel−Crafts Chemistry*; Wiley-Interscience: New York, 1973. (c) Heaney, H. *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, pp 733−752.

(17) For recent examples, see: Kobayashi, S.; Komoto, I.; Matsuo, J.-i. *Adv. Synth. Cat.* **2001**, *343*, 71 and references therein.

TABLE 9. Friedel–Crafts Acylation in the CO_2–6a System



Entry	Catalyst	Aromatics	Acylating Reagent	Conditions	Product	Yield (%)[a]
1	$Sc(OTf)_3$ (5 mol%)		AcCl	50 °C, 8 MPa, 6 h	 **8a**	64 (52)
2	$Sc(OTf)_3$ (5 mol%)		Ac_2O	50 °C, 8 MPa, 4 h	 **8b**	78 (71)
3	$Ga(OTf)_3$ (10 mol%)		BzCl	100 °C, 8 MPa, 6 h	 **8c**	quant (78)
4	$Ga(OTf)_3$ (10 mol%)		Ac_2O	50 °C, 15 MPa, 1 h	 **8d**	quant, 2-/3-isomer=93/7 (99, 2-/3-isomer=94/6)
5	$Ga(OTf)_3$ (10 mol%)		Ac_2O	100 °C, 8 MPa, 6 h	 **8e**	45 (25)

[a] Products yield without the additive are shown in parentheses. [b] **6a** (ca. 20 mg) was added in a 10 mL reaction vessel.

perfluoroalkyl chains of the catalysts and the surfactants influenced the yields of the products, and it was assumed that the reactants were packed in the media under highly concentrated conditions. This methodology provides a key to address the low reactivity issue of organic reactions in $scCO_2$ due to low solubility in CO_2.

Experimental Section

General Methods. Tetramethylsilane (TMS) served as internal standard ($\delta = 0$) for ^1H NMR, $CDCl_3$ was used as internal standard ($\delta = 77$) for ^{13}C NMR, and CF_3COOH was used as internal standard ($\delta = -76.5$) for ^{19}F NMR. Column chromatography was performed on silica gel 60 (Merck), and preparative thin-layer chromatography was carried out using Wakogel B-5F.

Materials. The perfluorobenzenes surfactants were prepared by the method described below. All reagents and solvents were used after purification according to usual methods.

Typical Experimental Procedure for the Aldol-Type Reaction in $scCO_2$–PEG System. Synthesis of Methyl 3-Benzylamino-2,2-dimethyl-3-phenylpropionate (3a).[18] $Yb(OTf)_3$ (16 mg, 0.026 mmol) and a small stirring bar were placed in a 10 mL stainless steel autoclave under argon atmosphere. Imine **1a** (103 mg, 0.53 mmol), silicon enolate **2a** (113 mg, 0.65 mmol), and poly(ethylene glycol) (44 mg, average $M_w = 400$) were mixed in a small ampule and put in the autoclave separately to prevent reactions under neat conditions before the autoclave was filled with CO_2. CO_2 was cooled at −10 °C and charged with an HPLC pump. During the introduction of CO_2, the autoclave was heated, and then pressure and temperature were adjusted to 15 MPa and 50 °C. The mixture was stirred for 3 h, the reactor was cooled with ice, and then the pressure was released. After hydrolytic workup with aqueous $NaHCO_3$ and ethyl ether, the organic layer was dried with anhydrous Na_2SO_4. After being concentrated, the residue was subjected to preparative TLC to give **3a** as a pale yellow oil (113 mg, 72% yield): ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H), 1.12 (s, 3 H), 3.64 (s, 3 H), 3.40 (d, $J = 13.2$ Hz, 1 H), 3.66 (d, $J = 13.2$ Hz, 1 H), 3.89 (s, 1 H), 7.19–7.38 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 19.4, 24.1, 47.4, 51.4, 51.8, 67.7, 126.8, 127.4, 127.9, 128.1, 128.2, 129.0, 139.1, 140.5, 177.7.

Methyl 2,2-dimethyl-3-phenyl-3-phenylaminopropionate (3b):[19] ^1H NMR ($CDCl_3$) δ 1.16 (s, 3 H), 1.27 (s, 3 H), 3.64 (s, 3 H), 4.49 (s, 1 H), 6.45–6.62 (m, 3 H), 6.99–7.07 (m, 2 H), 7.18–7.28 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 20.7, 24.5, 47.0, 52.0, 64.9, 113.4, 117.3, 127.4, 128.0, 128.3, 129.0, 139.2, 146.9, 177.0.

Methyl 2,2-dimethyl-5-phenyl-3-phenylamino-4-pentenoate (3c):[19] ^1H NMR ($CDCl_3$) δ 1.29 (s, 3 H), 1.32 (s, 3 H), 3.67 (s, 3 H), 4.13 (d, $J = 7.1$ Hz, 1 H), 6.09 (dd, $J = 7.2$, 15.8 Hz, 1 H), 6.55 (d, $J = 15.8$ Hz, 1 H), 6.63–6.70 (m, 3 H), 7.10–7.17 (m, 2 H), 7.19–7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 21.6, 23.5, 47.0, 52.0, 62.6, 113.7, 117.6, 126.5, 127.2, 127.6, 128.5, 129.2, 132.9, 136.7, 147.3, 177.0.

Methyl 3-(2′-furyl)-2,2-dimethyl-3-phenylaminopropionate (3d):[20] ^1H NMR ($CDCl_3$) δ 1.26 (s, 3 H), 1.27 (s, 3 H), 3.68 (s, 3 H), 4.71 (s, 1 H), 6.15 (d, $J = 3.2$ Hz, 1 H), 6.25 (dd, $J = 1.8$, 3.2 Hz, 1 H), 6.61–6.72 (m, 3 H), 7.09–7.15 (m, 2 H), 7.30 (dd, $J = 0.9$, 1.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.9, 23.6, 47.3, 51.6, 51.8, 61.5, 108.9, 109.9, 126.9, 128.1, 128.3, 140.2, 141.8, 153.6, 177.3.

***S*-Ethyl 3-(2′-methoxyphenylamino)-3-phenylpropanethioate (3e):**[7e] ^1H NMR ($CDCl_3$) δ 1.26 (s, 3 H), 1.27 (s, 3 H), 3.68 (s, 3 H), 4.71 (s, 1 H), 6.15 (d, $J = 3.2$ Hz, 1 H), 6.25 (dd, $J = 1.8$, 3.2 Hz, 1 H), 6.61–6.72 (m, 3 H), 7.09–7.15 (m, 2 H), 7.30 (dd, $J = 0.9$, 1.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.5, 23.5, 51.8, 55.4, 55.5, 109.4, 111.2, 116.9, 121.1, 126.3, 127.4, 128.7, 136.5, 142.0, 146.9, 197.0.

***S*-Ethyl 3-(2′-methoxyphenylamino)-2-methyl-3-phenylpropanethioate (3f)** (syn/anti = 57/43):[21] ^1H NMR ($CDCl_3$) δ 1.09 (t, $J = 7.3$ Hz, 3 H), 1.11 (d, $J = 7.3$ Hz, 1.29 H), 1.16 (t, $J = 7.4$ Hz, 1.29 H), 1.22 (d, $J = 7.0$ Hz, 1.71 H), 1.22 (t, $J = 7.2$ Hz, 1.29 H), 2.72–2.89 (m, 2 H), 2.94–3.10 (m, 1 H), 3.83 (s, 1.29 H), 3.85 (s, 1.71 H), 4.50 (d, $J = 7.7$ Hz, 0.43 H), 4.70 (d, $J = 5.7$ Hz, 0.57 H), 5.31 (brs, 1 H), 6.30 (dd, $J = 1.5$,

(18) Ipaktschi, J.; Heydari, A. *Chem. Ber.* **1993**, *126*, 1905.

(19) Akiyama, T.; Takaya, J.; Kagoshima, H. *Adv. Synth. Catal.* **2002**, *344*, 338.

(20) Ojima, I.; Inaba, S.; Nagai, M. *Synthesis* **1981**, 546.

(21) The configuration of the major diastereomer was assigned by transformation into the methyl ester derivative.

7.6 Hz, 0.57 H), 6.34 (dd, J = 1.5, 7.8 Hz, 0.43 H), 6.50−6.74 (m, 3 H), 7.14−7.32 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 12.4, 14.2, 14.5, 14.6, 15.9, 21.0, 23.3, 23.4, 54.75, 54.80, 55.57, 55.59, 60.0, 60.4, 60.9, 109.4, 109.5, 111.0, 111.3, 116.5, 116.8, 121.01, 121.04, 127.02, 127.03, 127.1, 127.2, 127.3, 127.4, 128.38, 128.44, 128.6, 136.7, 136.8, 140.9, 141.1, 146.9, 147.0, 201.5, 202.1; IR (neat) 3409, 2966, 2931, 1677, 1603, 1513, 1455, 1223, 1028, 963, 737, 702 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{19}H_{23}NO_2S$ (M^+) 329.1450, found 329.1425.

***S*-Ethyl 3-(2′-methoxyphenylamino)-2,2-dimethyl-3-phenylthiopropane thioate (3g):** ^{1}H NMR ($CDCl_3$) δ 1.17 (t, J = 7.4 Hz, 3 H), 1.23 (s, 3 H), 1.27 (s, 3 H), 2.83 (q, J = 7.4 Hz, 2 H), 3.85 (s, 3 H), 4.59 (s, 1 H), 5.29 (brs, 1 H), 6.28 (dd, J = 1.5, 7.6 Hz, 1 H), 6.55 (ddd, J = 1.5, 7.6, 7.6 Hz, 1 H), 6.62 (ddd, J = 1.5, 7.6, 7.6 Hz, 1 H), 6.70 (dd, J = 1.5, 7.6 Hz, 1 H), 7.18−7.33 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.4, 19.9, 23.3, 24.8, 53.5, 55.6, 64.6, 109.4, 110.9, 116.3, 121.1, 127.3, 127.9, 128.6, 137.0, 139.2, 146.9, 205.7; IR (neat) 3414, 2971, 2933, 1674, 1603, 1512, 1455, 1252, 1223, 947, 735, 706 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{20}H_{25}NO_2S$ (M^+) 343.1606, found 343.1599.

Methyl 3-(2′-methoxyphenylamino)-2-methyl-3-phenylpropionate (3h)[22] (syn/anti = 38/62 at Table 3, entry 8): ^{1}H NMR ($CDCl_3$) δ 1.14 (d, J = 7.1 Hz, 1.86 H), 1.21 (d, J = 7.3 Hz, 1.14 H), 2.83−2.92 (m, 0.62 H), 2.94−3.02 (m, 0.38 H), 3.59 (s, 1.14 H), 3.65 (s, 1.86 H), 3.86 (s, 1.86 H), 3.88 (s, 1.14 H), 4.51 (d, J = 7.8 Hz, 0.62 H), 4.73 (d, J = 5.4 Hz, 0.38 H), 5.04 (brs, 0.38 H), 5.28 (brs, 0.62 H), 6.33 (dd, J = 1.5, 7.8 Hz, 0.38 H), 6.40 (dd, J = 1.5, 8.0 Hz, 0.62 H), 6.57 (ddd, J = 1.5, 7.8, 7.9 Hz, 0.38 H), 6.59 (ddd, J = 1.5, 7.9, 8.0 Hz, 0.62 H), 6.65−6.76 (m, 2 H), 7.17−7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 12.1, 15.0, 46.5, 46.7, 51.75, 51.78, 55.6, 59.4, 60.5, 109.4, 109.5, 111.0, 111.1, 116.5, 116.6, 121.1, 126.8, 126.9, 127.2, 127.4, 128.4, 128.5, 136.79, 136.84, 140.9, 141.2, 146.9, 174.5, 175.3.

***S*-Ethyl 3-cyclohexyl-3-phenylaminopropanethioate (3i):** ^{1}H NMR ($CDCl_3$) δ 0.95−1.29 (m, 2 H), 1.19 (t, J = 7.4 Hz, 3 H), 1.50−1.92 (m, 9 H), 2.72 (dd, J = 6.7, 15.0 Hz, 1 H), 2.77 (dd, J = 5.6, 14.9 Hz, 1 H), 2.84 (q, J = 7.4 Hz, 2 H), 3.70−3.76 (m, 1 H), 6.61 (d, J = 8.1 Hz, 2 H), 6.66 (d, J = 7.3 Hz, 1 H), 7.14 (dd, J = 7.3, 8.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.6, 23.5, 26.2, 26.4, 29.1, 29.6, 41.9, 46.1, 55.8, 113.3, 117.3, 129.3, 147.4, 198.3; IR (neat) 3402, 3054, 3024, 2926, 2853, 1680, 1601, 1505, 1449, 1319, 1259, 745, 690 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{17}H_{25}NOS$ (M^+) 291.1657, found 291.1645.

Ethyl 3-cyclohexyl-3-phenylaminopropionate (3j): ^{1}H NMR ($CDCl_3$) δ 0.96−1.30 (m, 5 H), 1.18 (t, J = 7.1 Hz, 3 H), 1.47−1.93 (m, 6 H), 2.45 (dd, J = 7.0, 14.9 Hz, 1 H), 2.55 (dd, J = 5.2, 14.9 Hz, 1 H), 3.65−3.72 (m, 1 H), 4.06 (q, J = 7.1 Hz, 2 H), 6.59−6.69 (m, 3 H), 7.11−7.17 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 26.2, 26.4, 29.3, 29.4, 37.1, 42.1, 55.3, 60.4, 113.3, 117.1, 129.2, 129.2, 147.7, 172.3; IR (neat) 3393, 2926, 2851, 1732, 1602, 1509, 1280, 1187, 748, 692 cm^{-1}; MS (*m*/*z*) 275 (M^+). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.05; H, 9.08; N, 5.07.

Methyl 3-cyclohexyl-2,2-dimethyl-3-phenylaminopropanoate (3k):[19] ^{1}H NMR ($CDCl_3$) δ 1.00−1.26 (m, 4 H), 1.19 (s, 3 H), 1.23 (s, 3 H), 1.48−1.73 (m, 7 H), 3.50 (d, J = 3.9 Hz, 1 H), 3.65 (s, 3 H), 4.06 (brs, 1 H), 6.59−6.65 (m, 3 H), 7.10−7.16 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 22.6, 24.3, 26.1, 26.4, 26.8, 28.5, 32.9, 41.3, 47.3, 51.8, 64.0, 112.5, 116.4, 129.3, 149.7, 178.1.

1,3-Diphenyl-3-phenylaminopropan-1-one (3l):[19] ^{1}H NMR ($CDCl_3$) δ 3.41 (dd, J = 7.5, 16.1 Hz, 1 H), 3.50 (dd, J = 5.4, 16.1 Hz, 1 H), 5.00 (dd, J = 5.4, 7.5 Hz, 1 H), 6.54−6.58 (m, 2 H), 6.63−6.70 (m, 1 H), 7.06−7.11 (m, 2 H), 7.20−7.35 (m, 3 H), 7.40−7.58 (m, 5 H), 7.88−7.92 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 46.2, 54.9, 113.9, 117.9, 126.4, 127.4, 128.2, 128.7, 128.8, 129.1, 133.4, 136.6, 142.8, 146.7, 198.2.

3-Hydroxy-1,3-diphenyl-1-propanone (5a):[23] ^{1}H NMR ($CDCl_3$) δ 3.34 (d, J = 4.3 Hz, 1 H), 3.35 (d, J = 7.6 Hz, 1 H), 5.33 (dd, J = 4.3, 7.6 Hz, 1 H), 7.23−7.59 (m, 8 H), 7.91−7.94 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 47.4, 70.0, 125.7, 127.7, 128.1, 128.6, 128.7, 128.8, 133.7, 142.9, 200.2.

3-(4′-Chlorophenyl)-3-hydroxy-1-phenyl-1-propanone (5b):[23] ^{1}H NMR ($CDCl_3$) δ 3.34 (d, J = 5.8 Hz, 2 H), 3.63 (brs, 1 H), 5.32 (t, J = 5.8 Hz, 1 H), 7.26−7.43 (m, 4 H), 7.44−7.52 (m, 2 H), 7.56−7.63 (m, 1 H), 7.94 (d, J = 8.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 47.2, 69.4, 127.1, 128.1, 128.66, 128.72, 133.3, 133.7, 136.4, 141.4, 199.9.

3-Hydroxy-1-phenyl-3-(4′-methylphenyl)-1-propanone (5c):[23] ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3 H), 3.34−3.38 (m, 2 H), 3.51 (brs, 1 H), 5.32 (t, J = 5.9 Hz, 1 H), 7.19 (d, J = 7.9 Hz, 2 H), 7.33 (d, J = 7.9 Hz, 2 H), 7.43−7.50 (m, 2 H), 7.55−7.62 (m, 1 H), 7.93−7.98 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.1, 47.4, 69.9, 125.7, 128.1, 128.7, 129.2, 133.6, 136.6, 137.4, 140.0, 200.2.

Ethyl 3-hydroxy-3-phenylpropionate (5d):[24] ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 3 H), 2.70−2.80 (m, 2 H), 3.26 (brs, 1 H), 4.18 (q, J = 7.2 Hz, 2 H), 5.13 (dd, J = 4.4, 8.2 Hz, 1 H), 7.24−7.52 (m, 5 H), 7.25−7.33 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 43.3, 60.8, 70.3, 125.7, 127.8, 128.5, 142.5, 172.4.

Ethyl 3-hydroxy-5-phenyl-1-pent-4-enoate (5e):[25] ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.1 Hz, 3 H), 2.57−2.71 (m, 2 H), 3.06 (brs, 1 H), 4.19 (q, J = 7.1 Hz, 2 H), 4.72 (m, 1 H), 6.22 (dd, J = 6.2, 15.9 Hz, 1 H), 6.66 (d, J = 15.9 Hz, 1 H), 7.21−7.43 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.2, 41.5, 60.8, 68.9, 126.5, 127.8, 128.6, 129.9, 130.8, 136.4, 172.2.

Ethyl 3-hydroxy-5-phenyl-1-pentanoate (5f):[25] ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.2 Hz, 3 H), 1.64−1.92 (m, 2 H), 2.38−2.56 (m, 2 H), 2.64−2.88 (m, 2 H), 3.05 (d, J = 3.9 Hz, 1 H), 3.96−4.04 (m, 1 H), 4.17 (q, J = 7.2 Hz, 2 H), 7.15−7.32 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 31.7, 38.1, 41.3, 60.7, 67.2, 125.9, 128.40, 128.43, 141.7, 173.0.

Methyl 3-hydroxy-2-methyl-3-phenylpropionate (5g):[26] ^{1}H NMR ($CDCl_3$) syn isomer δ 1.12 (d, J = 7.1 Hz, 3 H), 2.79 (dq, J = 7.1, 4.1 Hz, 1 H), 3.67 (s, 3 H), 5.10 (d, J = 4.1 Hz, 1 H), 7.22−7.48 (m, 5 H), anti isomer δ 1.01 (d, J = 7.1 Hz, 3 H), 2.79 (dq, J = 8.4, 7.1 Hz, 1 H), 3.73 (s, 3 H), 4.75 (d, J = 8.4 Hz, 1 H), 7.20−7.48 (m, 5 H); ^{13}C NMR ($CDCl_3$) syn isomer δ 10.7, 46.3, 51.9, 73.6, 125.9, 127.5, 128.2, 141.4, 176.2, anti isomer δ 14.5, 47.1, 51.9, 76.4, 126.7, 128.1, 128.5, 141.5, 176.2.

***S*-Ethyl 3-hydroxy-3-phenylpropanethioate (5h):**[27] ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.4 Hz, 3 H), 2.89−3.05 (m, 5 H), 5.19 (d, J = 8.4 Hz, 1 H), 7.27−7.42 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.6, 23.5, 52.5, 70.9, 125.6, 127.9, 128.6, 142.3, 199.1.

***S*-Ethyl 3-hydroxy-2-methyl-3-phenylpropanethioate (5i)**[28] (syn/anti = 26/74): ^{1}H NMR ($CDCl_3$) δ 1.02 (d, J = 7.2 Hz, 2.22 H), 1.16 (d, J = 7.2 Hz, 0.78 H), 1.22 (t, J = 7.4 Hz, 0.78 H), 1.26 (t, J = 7.4 Hz, 2.22 H), 2.82−3.04 (m, 3 H), 4.81 (d, J = 8.3 Hz, 0.74 H), 5.11 (d, J = 4.0 Hz, 0.26 H), 7.26−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 11.3, 14.6, 15.5, 23.2, 23.3, 54.9, 55.4, 73.7, 76.6, 126.0, 126.6, 127.5, 128.1, 128.2, 128.5, 141.2, 141.6, 203.7, 204.1.

***S*-Ethyl 3-hydroxy-2,2-dimethyl-3-phenylpropanethioate (5j):**[29] ^{1}H NMR ($CDCl_3$) δ 1.11 (s, 3 H), 1.21 (s, 3 H), 1.25 (t, J = 7.4 Hz, 3 H), 2.87 (q, J = 7.4 Hz, 2 H), 4.93 (s, 1 H), 7.25−7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.4, 19.0, 23.3, 23.6, 54.3, 78.9, 127.7, 127.8, 139.9, 207.9.

***tert*-Butyl 3-hydroxy-2-methyl-3-phenylpropionate (5k)**[30] (syn/anti = 29/71): ^{1}H NMR ($CDCl_3$) δ 1.02 (d, J = 7.1 Hz, 2.13 H), 1.13 (d, J = 7.1 Hz, 0.87 H), 1.43 (s, 2.61 H), 1.47

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(s, 6.39 H), 2.76 (m, 0.71 H), 2.78−2.92 (m, 1 H), 2.97 (m, 0.29 H), 4.78 (dd, J = 3.8, 7.9 Hz, 0.71 H), 5.07−5.09 (m, 0.29 H), 7.23−7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 11.4, 15.5, 29.66, 29.70, 48.25, 48.35, 55.0, 55.6, 73.8, 76.7, 126.1, 126.6, 127.4, 128.0, 128.2, 128.4, 141.8, 175.3.

Isopropyl 3-hydroxy-2-methyl-3-phenylpropionate (5l)[31] (syn/anti = 37/63 in Table 4, entry 15): ^{1}H NMR ($CDCl_3$) δ 1.03 (d, J = 7.1 Hz, 1.89 H), 1.12 (d, J = 7.1 Hz, 1.11 H), 1.16 (d, J = 6.2 Hz, 1.11 H), 1.21 (d, J = 6.2 Hz, 1.11 H), 1.21 (d, J = 6.2 Hz, 1.89 H), 1.24 (d, J = 6.2 Hz, 1.89 H), 2.70−2.82 (m, 1 H), 3.04 (brs, 1 H), 4.74 (d, J = 8.2 Hz, 0.63 H), 5.00 (dq, J = 6.2, 6.2 Hz, 0.37 H), 5.06 (dq, J = 6.2, 6.2 Hz, 0.63 H), 5.07 (d, J = 4.2 Hz, 0.37 H), 7.24−7.38 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 11.0, 14.5, 21.61, 21.63, 21.66, 21.7, 46.5, 47.2, 68.07, 68.13, 73.7, 76.3, 126.1, 126.6, 127.4, 127.9, 128.2, 128.4, 141.4, 141.7, 175.4.

Phenyl 3-hydroxy-2-methyl-3-phenylpropionate (5m)[32] (syn/anti = 34/66): ^{1}H NMR ($CDCl_3$) δ 1.14 (d, J = 7.1 Hz, 1.98 H), 1.29 (d, J = 7.1 Hz, 1.02 H), 2.96−3.08 (m, 1 H), 4.83 (d, J = 8.6 Hz, 0.66 H), 5.13 (d, J = 5.0 Hz, 0.34 H), 6.84−6.89 (m, 1 H), 6.99−7.04 (m, 1 H), 7.13−7.22 (m, 1 H), 7.26−7.40 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 11.5, 14.4, 46.9, 47.4, 74.1, 76.4, 121.4, 121.5, 125.9, 126.2, 126.7, 127.8, 128.2, 128.4, 128.6, 129.37, 129.41, 141.4, 150.4, 150.5, 174.0, 174.3.

Preparation of 1-Dodecyloxy-4-heptadecafluorooctylbenzene (6a).[33,34] Into a 50 mL glass autoclave were added 0.30 g of 4-dodecyloxyiodobenzene (0.8 mmol), 5.54 g of 1-iodononafluorobutane (16 mmol), 1.02 g of activated copper (16 mmol), and 8 mL of pyridine, and the mixture was heated at 150 °C, 48 h. After being cooled to room temperature, 10 mL of water and 2 mL of 1 N aq HCl were added, and then the mixture was filtered with Celite and eluted with hexane. The filtrate was washed with 1 N aq HCl (30 mL × 5) and water (30 mL × 3). After drying with sodium sulfate, the mixture was purified by column chromatography (hexane) to give 139 mg of **6a** (0.29 mmol, 36% yield) as a white solid: mp 54−55 °C; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3 H), 1.24−1.50 (m, 18 H), 1.80 (dq, J = 6.9, 6.9 Hz, 2 H), 3.99 (t, J = 6.5 Hz, 2 H), 6.96 (d, J = 8.8 Hz, 2 H), 7.48 (d, J = 8.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.7, 26.0, 29.1, 29.4, 29.59, 29.63, 29.68, 29.71, 32.0, 68.3, 105−119 (m), 114.5, 120.6 (t, J = 24.8 Hz), 128.4 (t, J = 6.2 Hz), 162.0; ^{19}F NMR ($CDCl_3$) δ −126.4 (bs, 2 F), −123.0 (bs, 2 F), −122.2 (bs, 6 F), −121.6 (bs, 2 F), −110.0 (t, J = 14.6 Hz, 2 F), −81.1 (t, J = 10.0 Hz, 3 F); IR (KBr) 2921, 2853, 1615, 1518, 1475, 1370, 1257, 1211, 1144, 1112, 1090, 1051, 1017, 952, 845, 661, 559 cm^{-1}; MS (m/z) 680 (M^+). Anal. Calcd for $C_{26}H_{29}F_{17}O$: C, 45.89; H, 4.30. Found: C, 46.04; H, 4.60. After column chromatography, 150 mg of *p*-dodecyloxyiodobenzene was recovered (48% recovery).

1-Dodecyloxy-4-nonafluorobutylbenzene (6b): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3 H), 1.24−1.50 (m, 18 H), 1.80 (dq, J = 7.0, 7.0 Hz, 2 H), 3.99 (t, J = 6.6 Hz, 2 H), 6.97 (d, J = 8.8 Hz, 2 H), 7.48 (d, J = 8.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.7, 26.0, 28.9, 29.4, 29.57, 29.60, 29.6, 29.7, 31.9, 68.3, 106−120 (m), 114.4, 120.5 (t, J = 24.8 Hz), 128.4, 161.9; ^{19}F NMR ($CDCl_3$) δ −125.8- -126.1 (m, 2 F), −123.1- -123.3 (m, 2 F), −110.2 (dt, J = 2.8, 13.3 Hz, 2 F), −81.4 (ddt, J = 2.7, 2.7, 9.8 Hz, 3 F); IR (neat) 2927, 2853, 1614, 1519, 1466, 1349, 1232, 1135, 869, 826, 742, 686, 594, 526 cm^{-1}; HRMS (m/z) calcd for $C_{22}H_{29}F_9O$ (M^+) 480.2075, found 480.2058.

1-Dodecyloxybenzene (6c): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.7 Hz, 3 H), 1.24−1.50 (m, 18 H), 1.80 (dq, J = 6.7, 6.7 Hz, 2 H), 3.95 (t, J = 6.6 Hz, 2 H), 6.86−6.96 (m, 3 H), 7.25−7.33 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.7, 26.0, 29.27, 29.34, 29.4, 29.57, 29.59, 29.62, 29.65, 31.9, 67.8, 114.4, 120.4, 129.4, 159.1; IR (KBr) 2925, 2845, 1600, 1497, 1466, 1248, 1085, 1040, 750, 697 cm^{-1}.

1-Hexyloxy-4-heptadecafluorooctylbenzene (6d): mp 28−29 °C; ^{1}H NMR ($CDCl_3$) δ 0.91 (t, J = 9.0 Hz, 3 H), 1.30−1.53 (m, 6 H), 1.80 (dq, J = 7.0, 7.0 Hz, 2 H), 4.00 (t, J = 6.5 Hz, 2 H), 6.97 (d, J = 9.0 Hz, 2 H), 7.49 (d, J = 9.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.6, 25.7, 29.1, 31.5, 68.2, 107.0−116.8 (m), 114.4, 118.6 (t, J = 33.0 Hz), 120.5 (t, J = 24.8 Hz), 128.4 (t, J = 6.2 Hz), 161.9; ^{19}F NMR ($CDCl_3$) δ −126.4 (bs, 2 F), −123.0 (bs, 2 F), −122.2 (bs, 6 F), −121.6 (bs, 2 F), −110.0 (t, J = 14.8 Hz, 2 F), −81.1 (t, J = 10.0 Hz, 3 F); IR (KBr) 2941, 2869, 1615, 1521, 1473, 1202, 1155, 1105, 845, 652, 559 cm^{-1}; MS (m/z) 596 (M^+). Anal. Calcd for $C_{20}H_{17}F_{17}O$: C, 40.28; H, 2.87. Found: C, 40.00; H, 2.96.

1-Methoxy-4-heptadecafluorooctylbenzene (6e):[35] mp 28−30 °C; ^{1}H NMR ($CDCl_3$) δ 3.86 (s, 3 H), 6.99 (d, J = 8.9 Hz, 2 H), 7.51 (d, J = 8.9 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 55.3, 107.5−119.0 (m), 114.0, 120.9 (t, J = 24.8 Hz), 128.5 (t, J = 6.2 Hz), 137.7, 142.3, 162.4; ^{19}F NMR ($CDCl_3$) δ −126.4 (s, 2 F), −123.0 (s, 2 F), −122.2 (s, 6 F), −110.0 (t, J = 14.1 Hz, 2 H), −81.1 (t, J = 10.0 Hz, 3 F); IR (KBr) 2970, 2844, 1615, 1519, 1205, 1146, 1027, 842, 651, 560 cm^{-1}.

Typical Experimental Procedure for the Aldol-Type Reaction in scCO$_2$−Perfluoroalkylbenzene System. Sc(OTf)$_3$ (13 mg, 0.026 mmol), 1-dodecyloxy-4-heptadecafluorooctylbenzene **6a** (20 mg), and a small stirring bar were placed in a 10 mL stainless steel autoclave under argon atmosphere. Aldehyde **4a** (54 mg, 0.51 mmol) and silicon enolate **2i** (116 mg, 0.60 mmol) were mixed in a small ampule and put in the autoclave separately to prevent reactions under neat conditions before the autoclave was filled with CO_2. CO_2 was cooled at −10 °C and charged with a HPLC pump. During the introduction of CO_2, the autoclave was heated, and then pressure and temperature were adjusted to 15 MPa and 50 °C. The mixture was stirred for 3 h, the reactor was cooled with ice, and then the pressure was released. After hydrolytic workup with water and dichloromethane, the organic layer was dried with anhydrous Na_2SO_4. The aqueous layer was concentrated in vacuo to give a crystalline residue, which was dried under reduced pressure at 200 °C for 4 h to afford 13 mg (quantitive recovery) of Sc(OTf)$_3$ as colorless crystals. The organic layer was concentrated, and the residue was treated with an aq HCl/THF solution (10 mL, 1 N aq HCl/THF = 1:9) at 0 °C for 1 h. After addition of water, the mixture was extracted with dichloromethane and the organic layer was dried with anhydrous Na_2SO_4. After filtration and concentration, dichloromethane (5 mL) was added to the residue and extracted with perfluorohexanes (FC-72, 15 mL) several times. The fluorous layer was concentrated to give **6a** (20 mg, quantitative recovery). The dichloromethane layer was concentrated, and the residue was subjected to preparative TLC to give the aldol adduct **5a** as a pale yellow oil (92 mg, 80% yield).

4-(3′-Indolyl)-2-butanone (7a):[7d] ^{1}H NMR ($CDCl_3$) δ 2.05 (s, 3 H), 2.76 (t, J = 7.4 Hz, 2 H), 2.94−3.00 (m, 2 H), 6.86−6.89 (m, 1 H), 7.00−7.07 (m, 1 H), 7.08−7.14 (m, 1 H), 7.23−7.27 (m, 1 H), 7.48−7.53 (m, 1 H), 7.94 (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.3, 30.0, 44.1, 111.1, 115.1, 118.6, 119.2, 121.4, 122.0, 127.1, 136.3, 208.8.

3-(3′-Indolyl)-1,3-diphenyl-1-propanone (7b):[7d] ^{1}H NMR ($CDCl_3$) δ 3.71 (dd, J = 7.5, 16.7 Hz, 1 H), 3.81 (dd, J = 7.5, 16.7 Hz, 1 H), 5.06 (t, J = 7.1 Hz, 1 H), 6.94−7.02 (m, 2 H), 7.10−7.17 (m, 2 H), 7.21−7.44 (m, 8 H), 7.49−7.55 (m, 1 H), 7.90−7.94 (m, 2 H), 7.98 (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 38.2, 45.2, 111.1, 119.2, 119.4, 119.5, 121.4, 122.1, 126.3, 126.6, 127.8, 128.1, 128.4, 128.6, 133.0, 136.6, 137.1, 144.2, 198.6.

4-{3′-(1′-Methylindolyl)}-2-butanone (7c):[7d] ^{1}H NMR ($CDCl_3$) δ 2.13−2.17 (m, 3 H), 2.80−2.87 (m, 2 H), 3.01−3.08 (m, 2 H), 3.71−3.75 (m, 3 H), 6.82−6.86 (m, 1 H), 7.08−7.15

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(m, 1 H), 7.20−7.32 (m, 2 H), 7.55−7.61 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.2, 30.0, 32.5, 44.3, 109.2, 113.6, 118.65, 118.68, 121.5, 126.3, 127.5, 136.9, 208.7.

2-(3′-Indolyl)-2-phenyl-1-nitroethane (7d):[7d] ^{1}H NMR ($CDCl_3$) δ 4.92 (dd, J = 8.3, 12.3 Hz, 1 H), 5.04 (dd, J = 7.5, 12.3 Hz, 1 H), 5.17 (dd, J = 7.5, 8.4 Hz, 1 H), 6.96−7.00 (m, 1 H), 7.06 (ddd, J = 1.0, 7.1, 8.0 Hz, 1 H), 7.18 (ddd, J = 1.0, 7.1, 8.2 Hz, 1 H), 7.21−7.35 (m, 7 H), 7.43 (d, J = 8.0 Hz, 1 H), 8.04 (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 41.5, 79.5, 111.3, 114.3, 118.9, 119.9, 121.6, 122.6, 126.0, 127.5, 127.7, 128.9, 136.4, 139.1.

1′-Hydroxy-2′-acetonaphthone (8a):[36] ^{1}H NMR ($CDCl_3$) δ 2.69 (s, 3 H), 7.26 (d, J = 8.4 Hz, 1 H), 7.53 (ddd, J = 1.3, 7.0, 8.3 Hz, 1 H), 7.58−7.66 (m, 1 H), 7.63 (d, J = 8.3 Hz, 1 H), 7.75 (d, J = 8.0 Hz, 1 H), 8.46 (d, J = 8.3 Hz, 1 H), 14.02 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 26.9, 113.2, 118.3, 124.4, 124.9, 125.2, 125.9, 127.4, 130.0, 137.3, 162.5, 204.3.

2′-Methoxy-1′-acetonaphthone (8b):[37] ^{1}H NMR ($CDCl_3$) δ 7.89 (d, J = 9.2 Hz, 1 H), 7.80 (d, J = 8.1 Hz, 1 H), 7.76 (d, J = 8.1 Hz, 1 H), 7.48 (ddd, J = 1.5, 6.9, 8.1 Hz, 1 H), 7.37 (ddd, J = 1.2, 6.9, 8.1 Hz, 1 H), 7.29 (d, J = 9.2 Hz, 1 H), 3.98 (s, 3 H), 2.65 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 32.7, 56.4, 112.8, 123.6, 124.1, 125.1, 127.7, 128.1, 128.8, 130.3, 131.4, 153.9, 205.2.

2,4-Dimethylbenzophenone (8c):[38] ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.39 (s, 3 H), 7.05 (d, J = 7.8 Hz, 1 H), 7.11 (s, 1 H), 7.24 (d, J = 7.8 Hz, 1 H), 7.41−7.47 (m, 2 H), 7.54−7.60 (m, 1 H), 7.77−7.81 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.1, 21.4, 125.7, 128.3, 129.2, 130.1, 131.9, 132.8, 135.6, 137.3, 138.2, 140.6, 198.5.

1-Phenylsulfonylacetylpyrrole (8d):[39] ^{1}H NMR ($CDCl_3$) 2-isomer δ 2.35 (s, 3 H), 6.36 (dd, J = 3.2, 3.4 Hz, 1 H), 7.06 (dd, J = 1.7, 3.4 Hz, 1 H), 7.48−7.56 (m, 2 H), 7.57−7.64 (m, 1 H), 7.83 (dd, J = 1.7, 3.2 Hz, 1 H), 7.96−8.00 (m, 1 H), 8.00−8.03 (m, 1 H), 3-isomer δ 2.41 (s, 3 H), 6.69 (dd, J = 1.7, 3.3 Hz, 1 H), 7.16 (dd, J = 2.2, 3.3 Hz, 1 H), 7.64−7.70 (m, 1 H), 7.52−7.60 (m, 2 H), 7.75 (dd, J = 1.7, 2.2 Hz, 1 H), 7.90−7.93 (m, 1 H), 7.93−7.96 (m, 1 H); ^{13}C NMR ($CDCl_3$) 2- isomer δ 26.9, 110.4, 124.4, 128.1, 128.6, 130.4, 133.3, 133.6, 138.9, 185.7, 3-isomer δ 27.2, 112.4, 121.6, 124.5, 127.1, 129.4, 129.7, 134.6, 138.0, 192.8.

2′,4′,6′-Trimethylacetophenone (8e):[38] ^{1}H NMR ($CDCl_3$) δ 2.21 (s, 6 H), 2.27 (s, 3 H), 2.45 (s, 3 H), 6.83 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 19.1, 21.0, 128.4, 132.3, 138.3, 139.8, 208.6.

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Supporting Information Available: General experimental information, experimental details, and spectral data for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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