Short Stereoselective Route to γ-CF_3 Allylic Alcohols: Rearrangements with Creation of Quaternary CF_3-Substituted Carbons

Denis Bouvet,[†] Hamid Sdassi,[‡] Michèle Ourévitch,[†] and Danièle Bonnet-Delpon*,[†]

BioCIS, UPRES A-8076. Centre d'Etudes Pharmaceutiques, Rue J-B Clément, 92296 Châtenay-Malabry, France, and Université Chouaib Doukkali, Faculté des Sciences, El Jadida, Morocco

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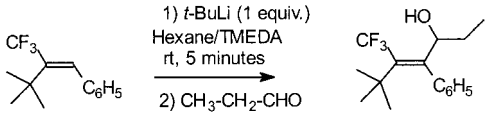
A concise preparation of tetrasubstituted hindered functionalized CF_3-olefins **2**−**7** from corresponding enol ether **3** is described. Geometrically pure γ-CF_3,γ-alkyl allylic alcohols thus prepared could undergo Claisen-type rearrangements and provide, in good yields, carboxylic esters and amides containing a β- quaternary CF_3-substituted carbon.

Claisen rearrangement and its variants found applications in the synthesis of trifluoromethylated compounds. Allyl vinyl ethers and allyl ketene silyl acetals, substituted with a trifluoromethyl group in the vinyl segment, readily undergo Claisen rearrangements and provide a good access to ramified trifluoromethyl ketones and α-CF_3 unsaturated acids, respectively.[1] γ-CF_3-allylic alcohols can be involved in Claisen,[2] Johnson−Claisen,[3] Eschenmoser−Claisen,[3] and Ireland−Claisen[4] rearrangements, which allowed the generation of secondary carbons, substituted with a trifluoromethyl group and a β functionality. To our knowledge, this potent tool has generally not been used to generate quaternary CF_3-substituted carbons, probably due to a lack of easy access to geometrically pure γ-CF_3, γ-alkyl allylic alcohols.[5] The Wittig condensation of trifluoromethyl ketones or trifluoroacetic anhydride with carbethoxy phosphoranes, leading to the corresponding α,β-unsaturated esters, is generally nonstereoselective.[6] Unlike the reduction of γ-CF_3 propargylic alcohols[7], other addition reactions to CF_3-substituted acetylenic compounds are poorly selective and have not been developed for the preparation of highly substituted allylic alcohols.[8] An alternative route to γ-CF_3 allylic alcohols is the trapping, with an electrophilic carbonyl compound, of β-metalated CF_3-substituted olefins. However, very little has been reported on this approach and no example concerns α,α-disubstituted olefins.[9] We have published as a preliminary result that the olefin **1a** could be metalated and react with propanal to give the allylic alcohol **2a** (Scheme 1).[10] We report here the development of this approach for a stereoselective access to functionalized hindered (trifluoromethyl)alkenes and Claisen-type rearrangements of thus prepared γ,γ-disubstituted allylic alcohols **2**.

Scheme 1



1a **2a**

Results and Discussion

Preparation of Allylic Alcohols 2a−c and 4a−c and Alkenes 6a and 7b. As previously reported, **1a** was found to react at room temperature with *tert*-butyllithium reagent (*t*-BuLi) in the presence of *N*,*N*,*N*′,*N*′-tetramethylenediamine (TMEDA) in hexane, and the resulting vinyl anion could be quenched with propanal, providing the allylic alcohol **2a**.[10] Since trisubstituted CF_3-olefins (*E*)-**1** were themselves stereoselectively prepared from the enol ether (*Z*)-**3**, through a carbolithiation−elimination reaction performed at −78 °C with alkyllithium reagents in tetrahydrofuran (THF) (Scheme 2),[10] we envisaged a one-pot stereoselective preparation of allylic alcohols from **3**.

We first checked that the carbolithiation−elimination reaction could occur at room temperature in hexane in the presence of TMEDA, which are the conditions of the metalation step. At room temperature, 1 equiv of *t*-BuLi reacted instantaneously with the enol ether **3** to provide

[†] BioCIS.

[‡] Université Chouaib Doukkali.

(1) Krespan, C. G. *Tetrahedron* **1967**, *23*, 4243−4249. (b) Yokozawa, T.; Nakai, T.; Ishikawa, N. *Tetrahedron Lett.* **1984**, *25*, 3991−3994. (c) Gajewski, J. J.; Gee, K. R.; Jurayj, J. *J. Org. Chem.* **1990**, *55*, 1813−1822. (d) Bégué, J. P.; Bonnet-Delpon, D.; Wu, S. W.; M'Bida, A.; Shintani, T.; Nakai, T. *Tetrahedron Lett.* **1994**, *35*, 2907−2910.

(2) Yamazaki, T.; Ishikawa, N. *Bull. Soc Chem. Fr.* **1986**, 937−943.

(3) Hanzawa, Y.; Kawagoe, K.; Yamada, A.; Kobayashi, Y. *Tetrahedron Lett.* **1985**, *26*, 219−222. (b) Konno, T.; Nakano, H.; Kitazume, T. *J. Fluorine Chem.* **1997**, *86*, 81−87.

(4) Konno, T.; Umetani, H.; Kitazume, T. *J. Org. Chem.* **1997**, *62*, 137−150

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(6) Camps, F.; Canela, R.; Coll, J.; Messeguer, A.; Roca, A. *Tetrahedron* **1978**, *34*, 2179−2182. (b) A.Shen, Y.; Xiang, Y. J. Fluorine Chem. **1991**, *52*, 221−227. (c) Martin V.; Molines, H.; Wakselman, C. *J. Fluorine Chem.* **1993**, *62*, 63−68.

(7) Hanzawa, Y.; Kawagoe, K.; Tanahashi, N.; Kobayashi, Y. *Tetrahedron Lett.* **1984**, *25*, 4749−4752. (b) Yamazaki, T.; Mizutani, K.; Kitazume, T. *J. Org. Chem.* **1995**, *60*, 6046−6056.

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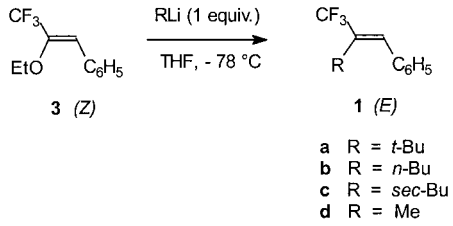
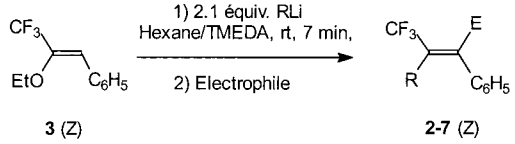
Scheme 2



3 (*Z*) **1** (*E*)

a R = *t*-Bu
b R = *n*-Bu
c R = *sec*-Bu
d R = Me

Scheme 3

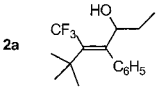
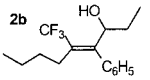
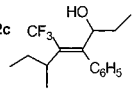
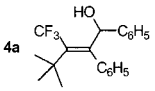
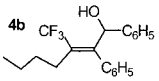
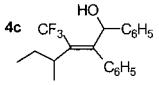
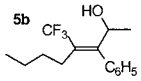
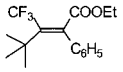
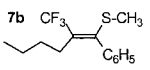


3 (Z) **2-7** (Z)

quantitatively the alkene (*E*)-**1a**. This confirms that, even under these new conditions, the deprotonation of **3** is not competitive with the carbolithiation reaction. The enol ether **3** was then treated with 2.1 equiv of *tert*-butyllithium, at room temperature in hexane in the presence of 2.1 equiv of TMEDA, and 1.2 equiv of propanal was added to the red solution of vinyl anion. After 1 h, the allylic alcohol **2a** was obtained, accompanied by alkene **1a** (about 80/20). An excess of base and aldehyde had only a slight influence on the course of the reaction, but the yield of **2a** was highly dependent on the time between addition of the organolithium reagent and that of aldehyde. A time of 7 min before the addition of the aldehyde appeared to be the best compromise to allow for the optimal formation of the vinyl anion and its trapping. Under these conditions, (*Z*)-**2a** could be obtained in 75% yield (Scheme 3, Table 1). This one-pot reaction was then extended to other organolithium reagents and to other electrophiles. We already knew that lithium amides could not be used in this reaction since they react with enol ether **3** to give corresponding enamines and do not allow the deprotonation of these latter.[11] Reaction of **3** with *n*-butyllithium or *sec*-butyllithium reagents and quenching, after 7 min, with propanal provided alcohols **2b** and **2c** in 83% and 82% yields, respectively, **2c** being a 50/50 mixture of two diastereoisomers (Scheme 3, Table 1). However, when the reaction was performed with methyllithium (MeLi), the only isolated compound was the olefin **1d**, indicating that MeLi is not a strong enough base to allow the metalation step.[12] When generated, vinyl anions could also be trapped with benzaldehyde and acetaldehyde, leading to alcohols **4a**−**c** and **5b** in excellent yields. Ethyl chloroformate and dimethyl sulfide could also act as electrophiles, providing the α-β unsaturated ester **6a** (R = *t*-Bu) and the vinyl sulfide **7b** (R = *n*-Bu) (Table 1).

All compounds were stereoselectively obtained. The *Z* configuration of the double bond in **4c** was demonstrated by NOE experiments. After complete assignment of protons by COSY heteronuclear multiple-quantum coherence (HMQC), and heteronuclear multiple bond coherence (HMBC), irradiation of fluorine atoms resulted in a 7% enhancement of the signal of the proton geminal to the hydroxy group. This effect indicates a spatial proximity of CF_3 and CHOH groups and demonstrates the *Z* configuration of the double bond. Furthermore, ^{13}C NMR spectra of all allylic alcohols exhibit a $^4J_{CF}$ coupling constant for the C(OH) carbon, indicating a proximity between the two nucleii. The stereochemistry was not unambiguously demonstrated for **6a** and **7b**.

Table 1. One-Pot Reaction of Vinyl Ether 3 with Organolithium Reagents and Trapping with Electrophiles

Entry	RLi	Electrophile	Compounds	Yield (%)[a]
a	*t*-BuLi	C_2H_5CHO	**2a** 	75 %
b	*n*-BuLi	C_2H_5CHO	**2b** 	83 %
c	*sec*-BuLi	C_2H_5CHO	**2c** 	82 %
d	*t*-BuLi	C_6H_5-CHO	**4a** 	95 %
e	*n*-BuLi	C_6H_5-CHO	**4b** 	85 %
f	*sec*-BuLi	C_6H_5-CHO	**4c** 	88 %
g	*n*-BuLi	CH_3CHO	**5b** 	88 %
h	*t*-BuLi	Cl-COOEt	**6a** 	79 %
i	*n*-BuLi	CH_3SSCH_3	**7b** 	75 %

[a] Isolated yield.

Rearrangements of Allylic Alcohols. (*Z*)-Allylic alcohols **2**−**5**, prepared as mentioned above, were subjected to ortho ester Johnson−Claisen and Eschenmoser−Claisen rearrangements.

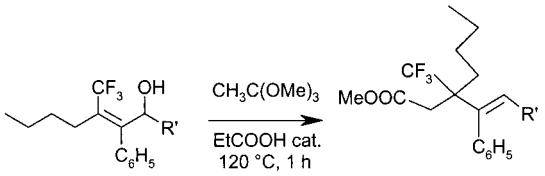
For the ortho ester rearrangement, reactions were conducted under conditions similar to that reported by Johnson[13] (an excess amount of methyl orthoacetate with 5 mol % of propionic acid heated to 120 °C). From **2b**, **4b**, and **5b**, rearranged β-CF_3 esters **8**, **9**, and **10** could be obtained, accompanied by a 10−20% mixture of starting allylic alcohol and other unidentified CF_3-substituted ethylenic compounds (according to their ^{19}F NMR chemical shifts). A higher temperature of reaction did not improve yields in esters. After purification, **8**, **9**, and **10** could be isolated in 80%, 68%, and 75% yields, respectively (Scheme 4). The *E* configuration of the newly formed carbon−carbon double bond was demonstrated by NMR experiments. After complete assignment as described above, homo- and heteronuclear Overhauser effects allow to identify the proximity of the ethylenic proton with other atoms: in **8**, with CF_3 and both methylene groups adjacent to the quaternary center; in

(11) Bégué, J−P.; Bonnet-Delpon, D.; Rock, M. H. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1409−1413.

(12) When **1d** was treated with BuLi, an undetermined mixture was obtained.

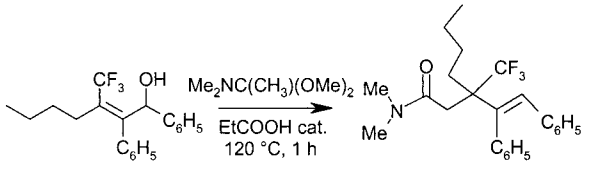
(13) Johnson, W. S.; Wetheman, L.; Bartlett, W. R.; Brockson, T. R.; Li, T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.

Scheme 4



8 R' = Et 80 %
9 R' = Ph 68 %
10 R' = Me 75 %

Scheme 5



4b **11**

9, with CF_3; in **10**, with methylene groups. In all cases, no traces of the *Z* isomer could be detected. This revealed that the rearrangement only proceeded via the sterically less hindered six-membered ring transition state, where the R′ substituent (Me, Et, or Ph) occupies the equatorial position. In previously described similar rearrangements, this isomer is always predominant but not the sole product.[2,3b]

The allylic alcohol **4b** could also undergo rearrangement after exposure to an amide acetal. According to literature conditions,[14] in the presence of an excess of 1-(dimethylamino)-1,1-dimethoxyethane and an equal volume of dry diglyme, at 160 °C, **4b** provided the amide **11** (75%) as a single stereoisomer at the newly created olefinic bond (Scheme 5). The *E* configuration was assigned as described for **8**−**10**.

We have described a short and effective access to functionalized and sterically hindered CF_3-substituted alkenes in two steps from trifluoroacetic esters. This method allowed the access to geometrically pure γ-CF_3, γ-alkyl allylic alcohols. When treated with an ortho ester or with an amide acetal, they easily rearranged into ester or amide with creation of a CF_3-substituted quaternary carbon and a stereoselective formation of new double bond.

Experimental Section

Alkenes **1** were already described.[10] Enol ether **3** was prepared from ethyl trifluoroacetate.[15]

Elemental analyses were performed by the Service de Microanalyses of the Centre d'Etudes Pharmaceutiques, Châtenay-Malabry. All the reactions were performed in an oven-dried apparatus under an inert atmosphere of argon. Commercial reagents were used without further purification.

General Procedure for the Preparation of Alkenes 2, 4, 5, 6, and 7. A solution of enol ether **3** (1 equiv) and TMEDA (2.1 equiv) in hexane was treated under argon with 2.1 equiv of alkyllithium at room temperature. A red color appeared, and after 7 min of stirring, 1.2 equiv of the electrophilic compound (propanal, benzaldehyde, ethyl chloroformate, dimethyldisulfure) (2.5 equiv for acetaldehyde) was introduced. After 1 h, the mixture was treated with a saturated solution of ammonium chloride. Organic phases were extracted with dichloromethane (3 × 20 mL), dried ($MgSO_4$), and evaporated to give a pale yellow oil that was purified by chromatography on silica gel (eluent: pentane/ether 90/10) to the pure compound.

(*Z*)-2,2-Dimethyl-5-hydroxy-4-phenyl-3-trifluoromethylhept-3-ene (2a). A solution of enol ether 3 (220 mg, 1 mmol), *tert*-butyllithium (1.4 mL of a 1.5 M solution in hexanes, 2.1 mmol), TMEDA (490 mg, 2.1 mmol) in hexane (10 mL), after addition of propanal (70 mg, 1.2 mmol), afforded, after workup and purification, the alcohol **2a** (210 mg, 75%): IR (CCl_4) 3640, 1635 cm^{-1}; ^{19}F NMR δ −48.9 (s); ^1H NMR δ 0.8 (t, J = 7 Hz, CH_3), 0.9 (s, 9 H), 1.5 (m, 2 H, CH_2), 4.6 (m, 1 H, C*H*OH), 6.9−7.2 (m, 5 H, C_6H_5); ^{13}C NMR δ 10.2, 28.9, 31.5, 37.2, 73.1 (q, $^4J_{CF}$ = 4.6 Hz, *C*HOH), 125.5 (q, $^1J_{CF}$ = 282 Hz, CF_3), 126.9, 127.0, 127.1, 129.7, 130.6, 135.2 (q, $^2J_{CF}$ = 23.5 Hz, *C*CF_3), 136.6, 149.2 (q, $^3J_{CF}$ = 2.9 Hz, *C*=CCF_3). Anal. Calcd for $C_{16}H_{21}F_3O$: C, 67.13; H, 7.34. Found: C, 67.30; H, 7.35

(*Z*)-3-Hydroxy-4-phenyl-5-trifluoromethylnon-4-ene (2b). A solution of enol ether **3** (220 mg, 1 mmol), *n*-butyllithium (1.3 mL of a 1.6 M solution in hexanes, 2.1 mmol), and TMEDA (490 mg, 2.1 mmol) in hexane (10 mL), after addition of propanal (70 mg, 1.2 mmol), afforded, after workup and purification, the alcohol **2b** (232 mg, 83%): ^{19}F NMR δ −55.7 (s); ^1H NMR δ 0.71 (t, J = 7 Hz, 3 H), 0.93 (d, J = 7.4 Hz, 3 H), 1.0−1.4 (m, 8 H), 1.6 (broad s, 1 H, OH), 4.75 (m, 1 H), 7.2 (m, 5 H, C_6H_5); ^{13}C NMR δ 10.3, 13.5, 22.5, 28.7, 29.5, 31.4, 71.8 (q, ^4J = 2.6 Hz), 124.8 (q, ^1J = 278 Hz, CF_3), 127.6, 128.1, 129.0, 130.2 (q, $^2J_{CF}$ = 28 Hz, C−CF_3), 135.9, 149.6. Anal. Calcd For $C_{16}H_{21}F_3O$: C, 67.13; H, 7.34. Found: C, 66.79; H, 7.66.

(*Z*)-3-Hydroxy-6-methyl-4-phenyl-5-trifluoromethyloct-4-ene (2c). A solution of enol ether **3** (220 mg, 1 mmol), *sec*-butyllithium (1.6 mL of a 1.5 M solution in hexanes, 2.1 mmol), and TMEDA (490 mg, 2.1 mmol) in hexane (10 mL), after addition of propanal (70 mg, 1.2 mmol), afforded, after workup and purification, the alcohol **2c** (232 mg, 82%): IR (neat) 3450, 1630 cm^{-1}; ^{19}F NMR δ −52.0 (s); ^1H NMR δ 0.65 (t, J = 7 Hz) and 0.7 (t, J = 7 Hz) (CH^3), 0.9 (m, J = 7. Hz, 6 H), 1.40 (m, 4 H), 2.20 (m, C*H*(CH_3)), 4.7 (m, C*H*OH), 7.2 (m, 5H); ^{13}C NMR δ 10.1/10.2, 12.4/12.5, 18.3/18.9, 27.1/27.3, 27.9, 38.1, 71.8 (q, $^4J_{CF}$ = 2.7 Hz), 125.0 (q, $^1J_{CF}$ = 292 Hz, CF_3), 127.4, 127.7, 127.9, 128.2, 128.3, 129.4, 132.8 (m, *C*CF_3), 136.1/136.6, 150.0 (q, $^3J_{CF}$ = 5.5 Hz). Anal. Calcd for $C_{16}H_{21}F_3O$: C, 67.13; H, 7.34. Found: C, 67.25; H, 7.33.

(*Z*)-4,4-Dimethyl-1,2-diphenyl-1-hydroxy-3-trifluoromethylpent-2-ene (4a). A solution of enol ether **3** (220 mg, 1 mmol), *tert*-butyllithium (1.4 mL of a 1.5 M solution in hexanes, 2.1 mmol), and TMEDA (490 mg, 2.1 mmol) in hexane (10 mL), after addition of benzaldehyde (132 mg, 1.2 mmol), afforded, after workup and purification, the alcohol **4a** (320 mg, 95%).

(*Z*)-1,2-Diphenyl-1-hydroxy-3-trifluoromethylhept-2-ene (4b). A solution of enol ether **3** (220 mg, 1 mmol), *n*-butyllithium (1.3 mL of a 1.6 M solution in hexanes, 2.1 mmol), and TMEDA (490 mg, 2.1 mmol) in hexane (10 mL), after addition of benzaldehyde (132 mg, 1.2 mmol), afforded, after workup and purification, the alcohol **4b** (238 mg, 83%).

(*Z*)-1,2-Diphenyl-1-hydroxy-4-methyl-3-trifluoromethylhex-4-ene (4c). A solution of enol ether **3** (220 mg, 1 mmol), *sec*-butyllithium (1.6 mL of a 1.5 M solution in hexanes, 2.1 mmol), and TMEDA (490 mg, 2.1 mmol) in hexane (10 mL), after addition of benzaldehyde (132 mg, 1.2 mmol), afforded, after workup and purification, the alcohol **4c** (298 mg, 88%).

(*Z*)-2-Hydroxy-3-phenyl-4-trifluoromethyl-oct-3-ene (5b). A solution of enol ether **3** (1 g, 4.6 mmol), *n*-butyllithium (6.1 mL of a 1.6 M solution in hexanes, 2.1 mmol), and TMEDA (2.254 g, 2.1 mmol) in hexane (40 mL), after addition of acetaldehyde (660 μL, 11.6 mmol), afforded, after workup and purification, the alcohol **5b** (1.1 g, 88%).

Ethyl (*Z*)-4,4-Dimethyl-2-phenyl-3-trifluoromethylpentenoate (6a). A solution of enol ether 2 (220 mg, 1 mmol), *tert*-butyllithium (1.4 mL of a 1.5 M solution in hexanes, 2.1 mmol), and TMEDA (490 mg, 2.1 mmol) in hexane (10 mL), after addition of ethyl chloroformate (132 mg, 1.2 mmol),

(14) Wick, A. E.; Felix, D.; Steen, K.; Eschenmoser, A. *Helv. Chim. Acta* **1964**, *47*, 2425.

(15) Bégué, J−P.; Bonnet-Delpon, D.; Mesureur, D.; Née, G.; Wu, S., W. *J. Org. Chem.* **1992**, *57*, 3807−3814.

afforded, after workup and purification and purification, the ester **6a** (242 mg, 79%): IR (neat) 1730, 1630 cm^{-1}; ^{19}F NMR δ −55.6 (s); ^1H NMR δ 1.0 (s, 9 H), 1.20 (t, J = 7.1 Hz, 3 H), 4.05 (q, J = 7.1 Hz, 2 H), 7.2 (m, 5 H); ^{13}C NMR δ 14.0, 29.5, 36.0, 61.5, 124.5 (q, $^1J_{CF}$ = 280 Hz, CF_3), 127.0, 128.2, 128.3, 130.2, 135.2 (q, $^2J_{CF}$ = 25.5 Hz, CCF_3), 136.0, 141.0 (q, $^3J_{CF}$ = 4.7 Hz $C{=}CCF_3$), 168.2 (CO). Anal. Calcd for $C_{16}H_{19}F_3O_2$: C, 64.00; H, 6.33. Found: C, 64.09; H, 6.50.

(*Z*)-1-Phenyl-1-thiomethyl-2-trifluoromethylhex-1-ene (7b). A solution of enol ether **2** (220 mg, 1 mmol), *n*-butyllithium (1.3 mL of a 1.6 M solution in hexanes, 2.1 mmol), and TMEDA (490 mg, 2.1 mmol) in hexane (10 mL), after addition of dimethyl disulfide (108 mg, 1.2 mmol), afforded, after workup and purification, **7b** (204 mg, 75%): IR (neat) 1665 cm^{-1}; ^{19}F NMR δ −59.1 (s); ^1H NMR δ 0.65 (t, J = 6.7 Hz, 3 H), 1.0 (m, 2 H), 1.25 (m, 2 H), 1.65 (s, CH_3S), 1.95 (t, J = 7.3 Hz, 2 H), 7.2 (m, 5H); ^{13}C NMR δ: 13.6, 15.7, 22.5, 30.7, 31.8, 124.5 (q, $^1J_{CF}$ = 278.7 Hz, CF_3), 128.1 (q, $^2J_{CF}$ = 32 Hz, $C{=}CF_3$), 128.4, 128.6, 128.7, 137.1, 144.8. Anal. Calcd for $C_{11}H_{17}SF_3$: C, 55.46; H, 7.14. Found: C, 55.40; H, 6.98.

Johnson−Claisen Rearrangement of Allylic Alcohols 2b, 4b, and 5b: General Procedure. A mixture of allylic alcohol, methyl orthoacetate (∼10 equiv), and a catalytic amount of propionic acid (1 drop) was heated in a flask at a vapor temperature of 110−120 °C until methanol no longer distilled from the reaction flask (about 1 h). After cooling, volatile material was removed under reduced pressure, and the crude product was purified by chromatography on a silica gel column (eluent: petroleum ether/ethyl acetate mixture 95/5).

Methyl (*E*)-3-Butyl-3-trifluoromethyl-4-phenylhept-4-enoate (8). From **2b**, (1.05 mmol, 300 mg), and methyl orthoacetate (1.1 mmol, 1.4 mL), reaction and workup afforded, after purification, the pure compound **8** as a colorless liquid (273 mg, 80%): ^{19}F NMR δ −71.2 (s); ^1H NMR δ 0.85 (t, J = 7.4 Hz, 3 H), 0.89 (t, J = 7.2 Hz, 3 H), 1.30−1.45 (m, 4 H), 1.66 (quint, J = 7.4 Hz, 2 H), 1.9 (m, 2 H), 2.56 and 2.64 (2d, ^2J = 15.3 Hz, 2 H), 3.6 (s, 3 H), 5.87 (tq, ^3J = 7.4 Hz, $^5J_{HF}$ = 0.9 Hz, 1 H, $C{=}CH$), 7.15 (m, 5 H, C_6H_5); ^{13}C NMR δ 13.7, 13.9, 23.1, 26.2, 31.6, 36.1, 50.5 (q, $^2J_{CF}$ = 23 Hz, $C{-}CF_3$), 51.5, 126.9, 127.8, 127.9 (q, $^1J_{CF}$ = 278 Hz, CF_3), 129.8, 129.9, 135.9, 136.8, 138.6, 170.5 ($C{=}O$). Anal. Calcd For $C_{19}H_{25}F_3O_2$: C, 66.65; H, 7.36. Found: C, 66.52; H, 7.54.

Methyl (*Z*)-3-Butyl-3-trifluoromethyl-4,5-diphenylpent-4-enoate (9). From **4b** (0.6 mmol, 200 mg) and methyl orthoacetate (1.1 mmol, 0.8 mL), reaction and workup afforded, after purification, the pure compound **9** as a colorless liquid (160 mg, 68%).

Methyl (*E*)-3-Butyl-3-trifluoromethyl-4-phenylhex-4-enoate (10). From **5b**, (1.1 mmol, 300 mg), and methyl orthoacetate (1.1 mmol, 1.4 mL), reaction and workup afforded, after purification, the pure compound **10** as a colorless liquid (258 mg, 75%).

Rearrangement of Eschenmoser−Claisen: Preparation of Methyl (*E*)-3-Butyl-3-trifluoromethyl-4,5-diphenylpent-4-ene-(*N*,*N*-dimethyl)amide (11). A mixture of the allylic alcohol **4b** (300 mg, 0.9 mmol) and *N*,*N*-dimethylacetamide (1 mL) in dry diglyme (1 mL) was heated in a 25 mL flask fitted with a variable takeoff distilling head. The distillate was removed at a vapor temperature of 160 °C, and after 2 h of additional heating, the solvent was removed under pressure. The yellow oil was purified by chromatography on silica gel (eluent: petroleum ether/EtOAc 95/5) to give the pure compound **11**, as a colorless oil (260 mg, 75%): ^{19}F NMR δ −71.1 (s); ^1H NMR δ.0.91 (t, J = 7.2 Hz, 3 H), 1.35 (m, 3 H), 1.5 (m, 1 H), 2.12 (ddd, ^2J = 14 Hz, ^3J = 11 Hz ^3J = 4 Hz, 1 H), 2.35 (td, ^2J = ^3J = 14 Hz ^3J = 4 Hz, 1 H), 2.65 and 2.70 (2d, ^2J = 16 Hz, 2 H), 2.85 (s, 6 H), 6.8 (s, 1 H, $C{=}CH$), 7.05 (m, 10 H); ^{13}C NMR δ 14.0, 23.2, 27.0, 32.5, 32.9, 35.6, 37.5, 51.3 (q, $^2J_{CF}$ = 22 Hz, $C{-}CF_3$), 126.8, 127.2, 127.7, 128.1, 128.5 (q, $^1J_{CF}$ = 285 Hz, CF_3), 129.4, 130.6, 132.2, 136.7, 138.9, 140.2, 169.1 ($C{=}O$). Anal. Calcd for $C_{24}H_{28}F_3NO$: C, 71.16; H, 6.99; N, 3.47. Found: C, 71.16; H, 7.19; N, 3.08.

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Supporting Information Available: Spectroscopic and analytical data for **4b**,**c**, **5b**, **6a**−**c**, **9**, and **10**. This material is available free of charge via the Internet at http:/pubs.acs.org.

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