Selective Cleavage and Decarboxylation of β-Keto Esters Derived from (Trimethylsilyl)ethanol in the Presence of β-Keto Esters Derived from Other Alcohols

Eva Knobloch, Reinhard Brückner*

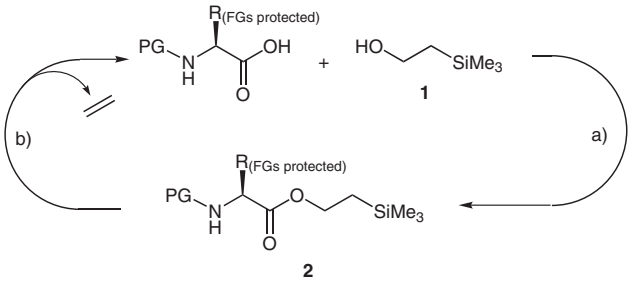
Institut für Organische Chemie und Biochemie, Albert-Ludwigs-Universität Freiburg, Albertstr. 21, 79104 Freiburg, Germany
Fax +49(761)2036100; E-mail: reinhard.brueckner@organik.chemie.uni-freiburg.de

Received 24 March 2008

Abstract: β-Keto[2-(trimethylsilyl)ethyl esters] are dealkoxycarbonylated at 50 °C by 0.75 equivalents of $Bu_4N^+F^-\cdot 3H_2O$ in THF. This reaction proceeds chemoselectively in the presence of β-keto(methyl esters), β-keto(*tert*-butyl esters), β-keto(allyl esters), or β-keto(benzyl esters) as revealed in intermolecular competition experiments.

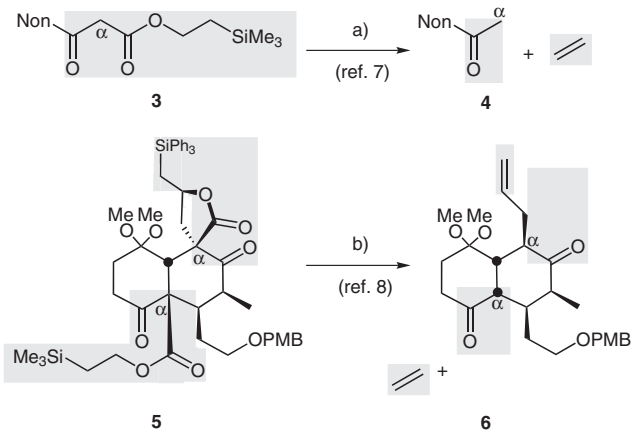
Key words: chemoselectivity, dealkoxycarbonylation, defunctionalization, β-keto esters, ketones

Thirty years ago CIBA-GEIGY reported that N-protected amino acids can be condensed with 2-(trimethylsilyl)ethanol (**1**; 'TMSE–OH') and that the resulting (trimethylsilyl)ethyl esters **2** ('TMSE esters') are cleaved at room temperature by treatment with 2–10 equivalents of anhydrous tetraalkylammonium tetrafluoroborates in DMF solution within 3–60 minutes (Scheme 1).[1] Since then, TMSE esters have been used as protecting groups repeatedly. The usual motivation is the desire to cleave TMSE esters by the already mentioned or other fluoride sources[2] without affecting other functionalities. In particular, TMSE ester were cleaved in the presence of methyl esters,[3] *tert*-butyl esters,[4] allyl esters,[5] and benzyl esters.[6] Arguably, $Bu_4N^+F^-\cdot 3H_2O$ (1.2–6 equiv) is the most common reagent used for this purpose (r.t., 4–16 h).[3–6]



Scheme 1[1] *Reagents and conditions*: a) protected amino acid, **1** (1.2 equiv), pyridine (2.0 equiv), DCC (1.1 equiv), MeCN, 0 °C, 6–16 h; b) **2** in DMF, $Bu_4N^+F^-$ or $Et_4N^+F^-$ (2–10 equiv) in DMSO, 24 °C, 3–60 min, then 0 °C, H_2O. FG = functional group.

β-Keto[(trimethylsilyl)ethyl esters] ['β-keto(TMSE esters)'] – present in substrates **3**[7] and **4**[8] of Scheme 2 – or the β-keto[(triphenylsilyl)ethyl ester] group incorporated into the substrate **5**,[7] can be cleaved by $Bu_4N^+F^-\cdot 3H_2O$, too, as we observed recently (Scheme 2). In these instances the ester cleavages proper were followed by an in situ decarboxylation of the respective β-keto carboxylic acid or corresponding β-keto carboxylate intermediate.



Scheme 2 Dealkoxycarbonylations of β-keto(TMSE esters) prior to the present study. *Reagents and conditions*: a) $Bu_4N^+F^-\cdot 3H_2O$ (2.0 equiv), THF, r.t., 8 h; 98%; b) $Bu_4N^+F^-\cdot 3H_2O$ (3.0 equiv), THF, r.t., 10 h, 64%. Non = *n*-C_9H_{19}; PMB = 4-$MeOC_6H_4CH_2$.

The reactions depicted in Scheme 2 exemplify a previously unrecorded transformation: the one-pot cleavage and decarboxylation – or dealkoxycarbonylation – of β-keto(TMSE esters) providing C_1-shortened ketones, for example, compounds **4** or **6**.

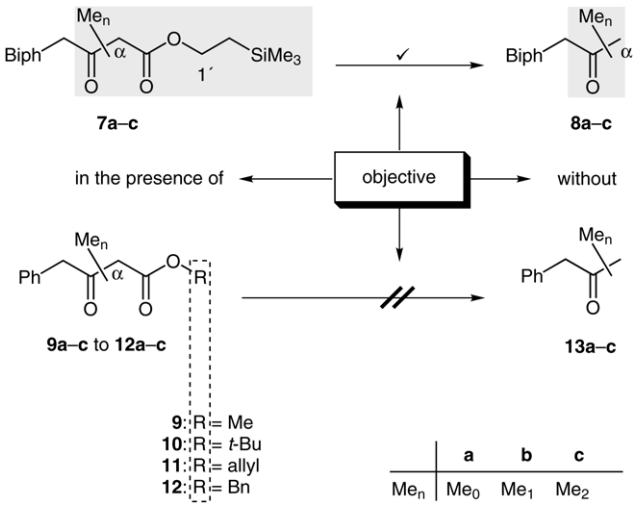
Investigating the scope and limitations of this process, we examined three aspects (Scheme 3):

• Do β-keto(TMSE esters) **7** in general dealkoxycarbonylate in the presence of $Bu_4N^+F^-\cdot 3H_2O$ and form C_1-shortened ketones **8** thereby?

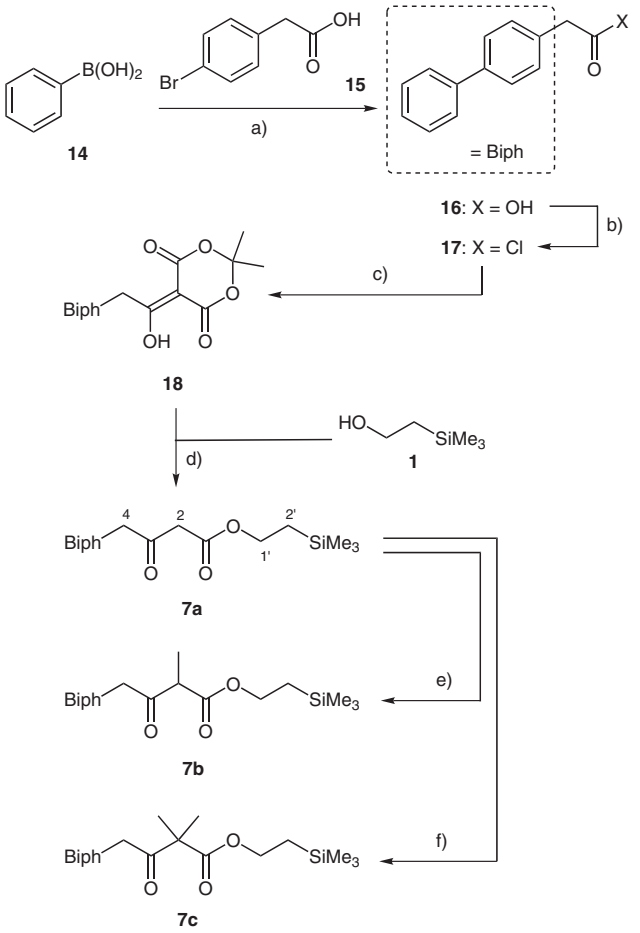
• Can the substitution pattern of the β-keto(TMSE esters) **7** be varied (**a**–**c**) such that ketones **8a**–**c** are obtained, which exhibit 0, 1, or 2 substituents at C-α?

• Are selective $Bu_4N^+F^-$-induced dealkoxycarbonylations of β-keto(TMSE esters) **7** possible in the presence of a β-keto ester derived from methanol (**9**), *tert*-butanol (**10**), allyl alcohol (**11**), or benzyl alcohol (**12**)?[9,10]

SYNLETT 2008, No. 12, pp 1865–1869
Advanced online publication: 02.07.2008
DOI: 10.1055/s-2008-1078568; Art ID: G10508ST



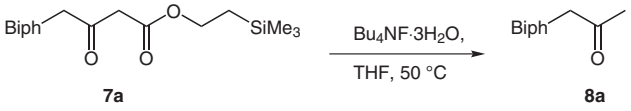
Scheme 3 Scope and limitations of one-pot β-keto(TMSE ester) cleavage–decarboxylation reactions. Biph = 4-PhC_6H_4 (biphenyl-4-yl)



Scheme 4 Syntheses of β-keto(TMSE esters) **7a–c**. *Reagents and conditions*: a) **14** (1.1 equiv), 5% Pd/C (3 mol%), Na_2CO_3 (1.3 equiv), H_2O–*i*-PrOH (6:1); 92% (ref.[13] 85%); b) $SOCl_2$ (11 equiv), DMF (10 mol%), toluene, 80 °C, 3 h; c) Meldrum's acid (1.0 equiv), pyridine (3 equiv), CH_2Cl_2, 0 °C to r.t., 18 h; d) **1** (1.1 equiv), toluene, 85 °C, 3.5 h; 86% (over the 3 steps); e) NaH (1.1 equiv), THF, 0 °C, 30 min; then r.t., MeI (1.1 equiv), 12 h; 84%; f) 2 × [NaH (1.1 equiv), THF, 0 °C, 30 min; then r.t., MeI (1.1 equiv), THF, 12 h]; 69%.

The β-keto(TMSE esters) **7a–c** were obtained as shown in Scheme 4. 4-Phenylphenylacetic acid (**16**) was prepared by a Pd/C-catalyzed[11] Suzuki coupling[12] between phenylboronic acid and 4-bromophenylacetic acid as published.[13] Acid **16** was converted into acid chloride **17**,[14] which was condensed without purification with Meldrum's acid. The resulting enol **18** was carried on one more step without purification: by (trimethylsily)ethanolysis and in situ decarboxylation. Purification by flash chromatography on silica gel[15] provided β-keto ester **7a** in 79% overall yield.[16] This compound was α-methylated by successive treatments with NaH and MeI.[17] The simple succession of these treatments delivered 84% α-methyl-β-keto ester **7b** and the double succession (without working up the intermediate, i. e. **7b**) α,α-dimethyl-β-keto ester **7c** in 69% yield. The silicon-free β-keto esters **9a–c** to **12a–c** were accessed by the same strategy.

Table 1 Cleavage and Decarboxylations of β-Keto(TMSE Ester) **7a** with Different Amounts of $Bu_4N^+F^-{\cdot}3H_2O$



Entry	$Bu_4N^+F^-{\cdot}3H_2O$ (equiv)	Time (h)	Yield (%)
1	1.0	1.25	94
2	0.75	2	100
3	0.5	2	89
4	0.25	8	84
5	0.1	8	–[a]

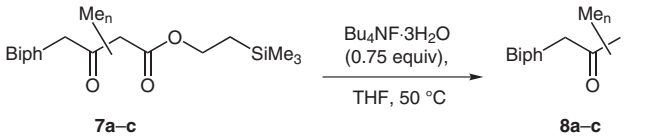
[a] After 8 h the ^{1}H NMR spectrum of the reaction mixture revealed the presence of starting material and product in a 52:48 ratio.

Three equivalents of $Bu_4N^+F^-{\cdot}3H_2O$ were required for cleaving and decarboxylating β-keto(TMSE ester) **7a** at room temperature. However, the reaction proceeded for 56 hours before we isolated 86% of the desired ketone **8a** but still retrieved 6% of unreacted substrate. Conducting the same reaction at 50 °C, an equimolar amount of $Bu_4N^+F^-{\cdot}3H_2O$ assured already a 94% yield of ketone **8a** after only 75 minutes (Table 1, entry 1). Substoichiometric amounts of $Bu_4N^+F^-{\cdot}3H_2O$ sufficed even for effecting the reaction, too (Table 1, entries 2–4): 0.75 equivalents thereof gave a perfect 100% yield after two hours, 0.5 equivalents gave 89% after 2 hours, and 0.25 equivalents gave 84% after 8 hours. The amount of 10 mol% of $Bu_4N^+F^-{\cdot}3H_2O$ effected ca. 50% cleavage and decarboxylation of keto ester **7a** within 8 hours (Table 1, entry 5). To the best of our knowledge, these findings are unprecedented in fluoride-mediated cleavages of simple TMSE esters.[1–6] The first dealkoxycarbonylations of β-keto(TMSE esters) **3**[7] and **5**[8] (cf. Scheme 1) did not anticipate these modified conditions either. The feasibility of such **7a** → **8a** conversions with as little as 25 mol% fluoride anions

implies that the Me_3Si group becomes incorporated not solely in Me_3Si–F but also – and sometimes mostly – in Si–O bond containing species (presumably Me_3Si–OH and/or Me_3Si–O–$SiMe_3$).

The α-methylated β-keto(TMSE esters) **7b**,**c** were dealkoxycarbonylated at 50 °C by 0.75 equivalents of $Bu_4N^+F^-\cdot 3H_2O$ in THF within 90 minutes almost as efficiently (Table 2, entries 2, 3) as the parent compound **7a** (Table 2, entry 1): Ketones **8b**,**c** were isolated in 90% and 82% yield, respectively.

Table 2 Cleavage and Decarboxylations of β-Keto(TMSE Esters) **7a–c** with 0.75 Equivalents of $Bu_4N^+F^-\cdot 3H_2O$



7a–c **8a–c**

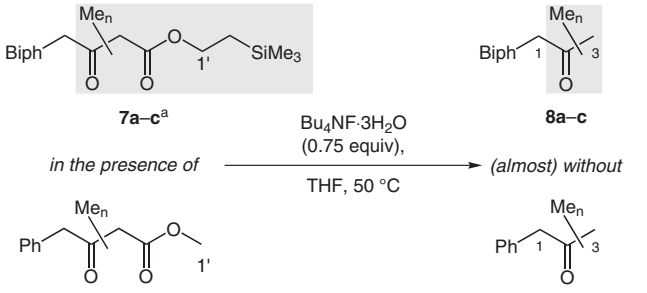
Substrate	Me_n	Time (h)	Yield (%)
7a	Me_0	2	100
7b	Me_1	1.5	90
7c	Me_2	1.5	82

The dealkoxycarbonylation procedure adopted in the experiments of Table 2 was then applied to pairs of β-keto esters (Tables 3– 6), one of them invariably being a β-keto(TMSE ester) **7**. All β-keto esters, which we exposed 'in competition' to the action of $Bu_4N^+F^-\cdot 3H_2O$[18] differed by their alkoxy groups but was identically α-methylated. The starting quantity of each keto ester was 0.2 mmol. Crude products were freed from side products by flash chromatography on silica gel[15] so that in each instance a pure mixture of up to two β-keto esters and up to two ketones was obtained. Its mass was determined and the kind and proportion of its constituents inferred by the assignment and integration of baseline-separated signals in its 300 MHz ^{1}H NMR spectrum.[19] The error margin for any yield calculated from these data[9] is estimated to be ≤±5%. This assessment is tantamount to accepting that the combined yields of a given substrate/product pair may be up to ±10% off the expected mass balance (100%) in the absence of side reactions and losses during the isolation procedure. Reassuringly, the yields presented in Tables 3– 6 stay within these margins.

In complete agreement with a number of chemoselective cleavages of simple TMSE esters with $Bu_4N^+F^-\cdot 3H_2O$ performed in substrates containing additionally a simple methyl ester,[3] *tert*-butyl ester,[4] allyl ester,[5] or benzyl ester,[6] the results of Tables 3– 6 document that β-keto(TMSE esters) can be cleaved and decarboxylated by $Bu_4N^+F^-\cdot 3H_2O$ as chemoselectively if a β-keto(methyl ester), a β-keto(*tert*-butyl ester), a β-keto(allyl ester), or a β-keto(benzyl ester) is present concomitantly.

In more detail, each of the β-keto(TMSE esters) **7a–c** was converted completely into the corresponding ketone **7a**,

Table 3 Intermolecularly Competing Dealkoxycarbonylations in Mixtures of β-Keto(TMSE esters) **7a–c** and β-Keto(methyl esters) **9a–c**



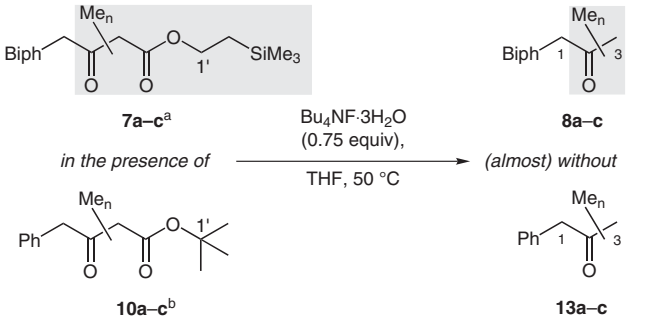
7a–c[a] **8a–c**

9a–c[b] **13a–c**

Entry	**7**–**9**, **13**	Me_n	Time (h)	Yields (%)[c] of re-isolated β-keto esters and resulting ketones			
				7 → **8**		**9** ⇸ **13**	
1	**a**	Me_0	3.5	0	98	97	5
2	**b**	Me_1	1.5	0	100	88	0
3	**c**	Me_2	1.5	0	99	99	0

[a] Enol contents in $CDCl_3$: **7a**, 10%; **7b**, 9%.
[b] Enol contents in $CDCl_3$: **9a**, 9%; **9b**, 5%.
[c] Determined ^{1}H NMR spectroscopically in $CDCl_3$[19] after separation of the **7**/**8**/**9**/**13** mixture from side products by flash chromatography on silica gel.[15]

Table 4 Intermolecularly Competing Dealkoxycarbonylations in Mixtures of β-Keto(TMSE esters) **7a–c** and β-Keto(*tert*-butyl esters) **10a–c**



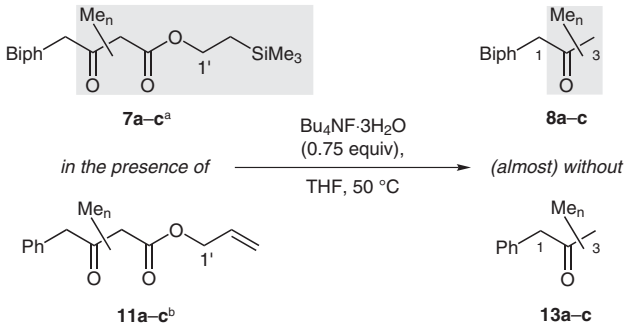
7a–c[a] **8a–c**

10a–c[b] **13a–c**

Entry	**7**, **8**, **10**, **13**	Me_n	Time (h)	Yields (%)[c] of re-isolated β-keto esters and resulting ketones			
				7 → **8**		**10** ⇸ **13**	
1	**a**	Me_0	3.5	0	98	98	0
2	**b**	Me_1	1.5	0	100	95	0
3	**c**	Me_2	1.5	0	99	103	0

[a] Enol contents in $CDCl_3$: **7a**, 10%; **7b**, 9%.
[b] Enol contents in $CDCl_3$: **10a**, 1%; **10b**, 3%.
[c] Determined ^{1}H NMR spectroscopically in $CDCl_3$[19] after separation of the **7**/**8**/**10**/**13** mixture from side products by flash chromatography on silica gel.[15]

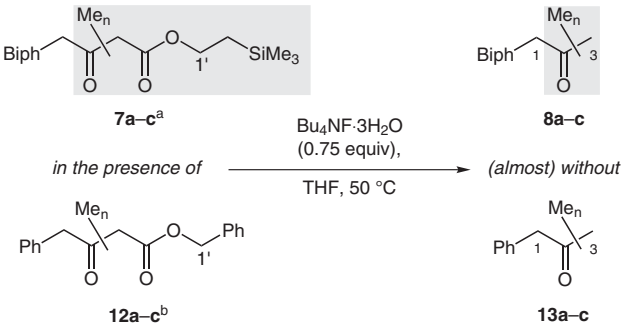
Table 5 Intermolecularly Competing Dealkoxycarbonylations in Mixtures of β-Keto(TMSE Esters) **7a–c** and β-Keto(allyl Esters) **11a–c**



Entry	7, 8, 11, 13	Me$_n$	Time (h)	Yields (%)[c] of re-isolated β-keto esters and resulting ketones			
				7 → 8		11 ⇸ 13	
1	**a**	Me$_0$	3.5	0	98	98	<5[d]
2	**b**	Me$_1$	1.5	0	100	95	0
3	**c**	Me$_2$	1.5	0	99	103	0

[a] Enol contents in $CDCl_3$: **7a**, 10%; **7b**, 9%.
[b] Enol contents in $CDCl_3$: **11a**, 9%; **11b**, 5%.
[c] Determined ^{1}H NMR spectroscopically in $CDCl_3$[19] after separation of the **7**/**8**/**11**/**13** mixture from side products by flash chromatography on silica gel.[15]
[d] This value is meant to indicate that the presence of ketone **13** did not follow unequivocally from the ^{1}H NMR spectrum.

Table 6 Intermolecularly Competing Dealkoxycarbonylations in Mixtures of β-Keto(TMSE Esters) **7a–c** and β-Keto(benzyl Esters) **12a–c**



Entry	7, 8, 12, 13	Me$_n$	Time (h)	Yields (%)[c] of re-isolated β-keto esters and resulting ketones			
				7 → 8		12 ⇸ 13	
1	**a**	Me$_0$	3.5	0	100	95	<5[d]
2	**b**	Me$_1$	1.5	0	105	95	0
3	**c**	Me$_2$	1.5	0	90	100	0

[a] Enol contents in $CDCl_3$: **7a**, 10%; **7b**, 9%
[b] Enol contents in $CDCl_3$: **12a**, 8%; **12b**, 9%
[c] Determined ^{1}H NMR spectroscopically in $CDCl_3$[19] after separation of the **7**/**8**/**12**/**13** mixture from side products by flash chromatography on silica gel;[15,]
[d] This value is meant to indicate that the presence of ketone **13a** did not follow unequivocally from the ^{1}H NMR spectrum

7b, or **7c**, whereas their β-keto(methyl ester) counterparts **9a–c** provided the underlying ketone **9a**, **9b**, or **9c** not all or in only 5% yield (Table 3). Similarly, the β-keto(TMSE esters) **7a–c** were defunctionalized by $Bu_4N^+F^-{\cdot}3H_2O$ completely – rendering the corresponding ketones **8a–c** in 89–98% yield – while the analogous β-keto(*tert*-butyl esters) **10a–c** stayed untouched (Table 4). Likewise, the β-keto(TMSE esters) **7a–c** and $Bu_4N^+F^-{\cdot}3H_2O$ provided the expected ketones **8a–c** in quantitative yields – in contrast to the β-keto(allyl esters) **11a–c**, which remained inert (Table 5). Finally, ketones **8a–c** formed from β-keto(TMSE esters) **7a–c** and $Bu_4N^+F^-{\cdot}3H_2O$ in ≥90% yield whereas the equally present β-keto(benzyl esters) **12a–c** were retrieved in essentially quantitative yields (Table 6).

In summary, we have shown how β-keto(TMSE esters) can be dealkoxycarbonylated chemoselectively in the presence of a β-keto(methyl ester), a β-keto(*tert*-butyl ester), a β-keto(allyl ester), or a β-keto(benzyl ester). Whether, in an extension of the present findings, one may regard β-keto(TMSE esters) as orthogonally protected β-keto esters vs. β-keto esters derived from methanol, *tert*-butanol, allyl alcohol, or benzyl alcohol, is a matter of current study in our laboratory. This additional attribute would be justified if the latter β-keto esters can be dealkoxycarbonylated under conditions, which leave a β-keto(TMSE ester) intact.

References and Notes

(1) Sieber, P. *Helv. Chim. Acta* **1977**, *60*, 2711.
(2) Wuts, P. G.; Greene, T. W. *Protective Groups in Organic Synthesis*, 4th ed.; John Wiley and Sons: New York, **2007**, 576.
(3) Chemoselective deprotection of TMSE esters besides methyl esters (representative examples): (a) Jung, M.; Miller, M. J. *Tetrahedron Lett.* **1985**, *26*, 977. (b) Bailey, S.; Teerawutgulrag, A.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1995**, 2521. (c) Travins, J. M.; Etzkorn, F. A. *J. Org. Chem.* **1997**, *62*, 8387. (d) Hu, T.; Panek, J. S. *J. Am. Chem. Soc.* **2002**, *124*, 11368. (e) Tripp, J. C.; Schiesser, C. H.; Curran, D. P. *J. Am. Chem. Soc.* **2005**, *127*, 5518. (f) Bailey, S.; Helliwell, M.; Teerawutgulrag, A.; Thomas, E. J. *Org. Biomol. Chem.* **2005**, *3*, 3654.
(4) Chemoselective deprotection of TMSE esters besides *tert*-butyl esters (representative examples): (a) Liu, G.; Xin, Z.; Liang, H.; Abad-Zapatero, C.; Hayduk, P. J.; Janowick, D. A.; Szczepankiewicz, B. G.; Pei, Z.; Hutchins, C. W.; Ballaron, S. J.; Stashko, M. A.; Lubben, T. H.; Berg, C. E.; Rondinone, C. M.; Trevillyan, J. M.; Jirousek, M. R. *J. Med. Chem.* **2003**, *46*, 3437. (b) Seebach, D.; Kimmerlin, T.; Šebasta, R.; Campo, M. A.; Beck, A. K. *Tetrahedron* **2004**, *60*, 7455.
(5) Chemoselective deprotection of TMSE esters besides allyl esters (representative examples): (a) Scheidt, K. A.; Chen, H.; Follows, B. C.; Chemler, S. R.; Coffey, D. S.; Roush, W. R. *J. Org. Chem.* **1998**, *63*, 6436. (b) Bourne, G. T.; Meutermans, W. D. F.; Alewood, P. F.; McGeary, R. P.;

Scanlon, M.; Watson, A. A.; Smythe, M. L. *J. Org. Chem.* **1999**, *64*, 3095.

(6) Chemoselective deprotection of TMSE esters besides benzyl esters (representative examples): (a) Cuenoud, B.; Schepartz, A. *Tetrahedron* **1991**, *47*, 2535. (b) Dietrich, A.; Wrobel, J. *Tetrahedron Lett.* **1993**, *34*, 3543. (c) Sundaramoorthi, R.; Siedem, C.; Vu, C. B.; Dalgarno, D. C.; Laird, E. C.; Botfield, M. C.; Combs, A. B.; Adams, S. E.; Yuan, R. W.; Weigele, M.; Narula, S. S. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1665. (d) Venturi, F.; Venturi, C.; Liguori, F.; Cacciarini, M.; Montalbano, M.; Nativi, C. *J. Org. Chem.* **2004**, *69*, 6153.

(7) Kramer, R. *Dissertation*; Universität Freiburg: Germany, **2007**, 279–280.

(8) Tricotet, T.; Brückner, R. *Eur. J. Org. Chem.* **2007**, 1069.

(9) After treatment with $Bu_4N^+F^-\cdot 3H_2O$, any such experiment could 'rightfully' (i. e., in the absence of side reactions) deliver a mixture of up to four components, namely the unconsumed β-keto esters and the resulting ketones. We distinguished them by ^{1}H NMR spectroscopy (ref. 10) and quantified their relative amounts by integration of non-superimposed resonances. In addition, we determined the absolute amounts (i. e., absolute yields) of these species by weighing the respective mixture. Thereupon, the mole fraction of each component, its molecular weight, and the gram amount of the mixture allowed for the yields listed in Tables 3– 6 to be calculated.

(10) As remote and modest as the aryl group variation in the resulting ketones **8a**–**c** vs. **13a**–**c** may appear, the chemical shift effect accompanying it sufficed for differentiating, among others, the following resonances: $\delta_{3\text{-}H_3} = 2.20$ in **8a** vs. 2.15 in **13a**; $\delta_{3\text{-}H_2} = 2.51$ in **8b** vs. 2.47 in **13b**; $\delta_{1\text{-}H_2} = 3.78$ in **8c** vs. 3.74 in **13c**. The β-keto esters were distinguished from the ketone(s) by their alkoxy resonances.

(11) Felpin, F.-X.; Ayad, T.; Mitra, S. *Eur. J. Org. Chem.* **2006**, 2679.

(12) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633. (c) Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem. Int. Ed.* **2001**, *40*, 4544; *Angew. Chem.* **2001**, *113*, 4676. (d) Miyaura, N. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; de Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weinheim, **2004**, 41–124. (e) Bellina, F.; Carpita, A.; Rossi, R. *Synthesis* **2004**, 2419.

(13) Gala, D.; Stamford, A.; Jenkins, J.; Kugelman, M. *Org. Process Res. Dev.* **1997**, *1*, 163.

(14) All new compounds gave satisfactory ^{1}H NMR and ^{13}C NMR spectra and provided correct combustion analyses (C and H ± 0.4%).

(15) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(16) The crude acylation product **18** (1.3 g, 3.8 mmol) was dissolved in toluene (10 mL). Alcohol **1** (0.60 mL, 0.50 g, 4.2 mmol, 1.1 equiv) was added within 5 min. The mixture was stirred at 80 °C for 3.5 h. Evaporation of the solvent under reduced pressure and flash chromatography on SiO_2 (see ref. 15; eluent: cyclohexane–EtOAc, 15:1) provided a mixture of the two tautomers of 2-(trimethylsilyl)ethyl 4-(4-phenylphenyl)-3-oxobutanoate (**7a**; 1.324 g, 94%) as a faintly yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$; 90:10 mixture of keto and enol tautomer): δ = 0.06 [s, $Si(CH_3)_3$ (**7a**)], 0.06 [s, $Si(CH_3)_3$ (enol-**7a**)], 1.02 [m_c, 2′-H_2 (**7a** and enol-**7a**)], 3.43 [s, 4-H_2 (**7a**)], 3.56 [s, 4-H_2 (enol-**7a**)], 3.90 [s, 2-H_2 (**7a**)], 4.25 [m_c, 1′-H_2 (**7a** and enol-**7a**)], 4.99 [m_c, 2-H (enol-**7a**)], 7.27–7.61 [m, Ar-H (**7a** and enol-**7a**)], 12.23 [s, 3-OH (enol-**7a**)]. Anal. Calcd (%) for $C_{21}H_{26}O_3Si$ (354.5): C, 71.15; H, 7.39. Found: C, 70.90; H, 7.40.

(17) Reaction conditions were gleaned from a protocol by: Hogan, F.; Herald, D. L.; Petit, G. R. *J. Org. Chem.* **2003**, *69*, 4019.

(18) **General Procedure for the Execution of the Competition Experiments Listed in Tables 3–6**
At 0 °C $Bu_4N^+F^-\cdot 3H_2O$ (47 mg, 0.15 mmol, 0.75 equiv) in THF (0.5 mL) was added dropwise to a mixture of one of the β-keto(TMSE esters) **7a**–**c** (0.20 mmol) and another β-keto ester **9a**–**c** to **12a-c** (0.20 mmol) in THF (1.5 mL). The resulting mixture was stirred at 50 °C until conversion was complete as judged by TLC. Brine (1.5 mL), H_2O (3 mL), and *t*-BuOMe (3 mL) were added. Extraction with *t*-BuOMe (3 × 3 mL), drying of the combined extracts with Na_2SO_4, evaporation of the solvent under reduced pressure, and flash chromatography on SiO_2 (ref. 15; eluent: cyclohexane–EtOAc) furnished a mixture of unreacted β-keto ester(s) and newly formed ketone(s) devoid of any byproducts. The yield of each component was determined as described in refs. 9 and 19.

(19) The mole fractions of the β-keto ester and ketone constituents of each mixture isolated from one of the experiments summarized in Tables 3– 6 were inferred from the integral ratios over the following ^{1}H NMR resonances (300 MHz, $CDCl_3$): **7a**: δ = 4.22 (m_c, 1′-H_2); **7b**: δ = 4.20 (m_c, 1′-H_2); **7c**: δ = 4.21 (m_c, 1′H_2); **8a**: δ = 2.20 (s, 3-H_3); **8b**: δ = 2.51 (q, $J_{3,4}$ = 7.2 Hz, 3-H_2); **8c**: δ = 3.78 (s, 1-H_2); **9a**: δ = 3.64 (s, 1′-H_3); **9b**,**c**: δ = 3.70 (s, 1′-H_3); **10a**–**c**: δ = 1.46 [s, 1′-$(CH_3)_3$]; **11a**: δ = 4.61 (ddd, $J_{1',2'}$ = 5.8 Hz, $^4J_{1',3'(E)} = {}^4J_{1',3'(Z)}$ = 1.4 Hz, 1′-H_2); **11b**,**c**: δ = 4.60 (ddd, $J_{1',2'}$ = 5.8 Hz, $^4J_{1',3'(E)} = {}^4J_{1',3'(Z)}$ = 1.4 Hz, 1′-H_2); **12a**,**c**: δ = 5.15 (s, 1′-H_2); **12b**: δ = 5.14 (s, 1′-H_2); **13a**: δ = 2.15 (s, 3-H_3); **13b**: δ = 2.47 (q, $J_{3,4}$ = 7.3 Hz, 3-H_2); **13c**: δ = 3.74 (s, 1-H_2). The β-keto ester signals compiled above coincide for the respective keto and enol tautomers if the substitution pattern **a** is realized and for compound **10b**; the enol resonances corresponding to the signals specified for keto tautomers **7b**, **9b**, **11b**, and **12c** are shifted downfield by 0.06 ppm.