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Mild and Efficient Pentafluorophenylammonium Triflate (PFPAT)-Catalyzed C-Acylations of Enol Silyl Ethers or Ketene Silyl (Thio)Acetals with Acid Chlorides

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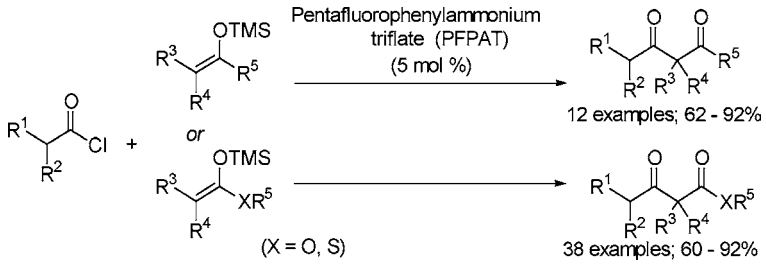
ABSTRACT



A pentafluorophenylammonium triflate (PFPAT) catalyst (5 mol %) successfully promoted C-acylation of enol silyl ethers with acid chloride to produce various β-diketones (12 examples; 62–92% yield). Similarly, C-acylation of ketene silyl acetals or ketene silyl thioacetals (i.e., crossed Claisen condensation) proceeded smoothly to provide not only α-monoalkylated β-keto (thio)esters but also thermodynamically unfavorable (less accessible) α,α-dialkylated β-keto (thio)esters in good to excellent yield (38 examples; 60–92% yield).

Regio- and chemoselective C-acylation of the α-position of carbonyl compounds is recognized as a fundamental and useful C−C bond forming reaction for obtaining 1,3-dicarbonyl compounds in organic syntheses.[1] There are a number of useful catalytic carbon−carbon bond forming reactions using enol silyl ethers, ketene silyl acetals (KSAs), and ketene silyl thioacetals (KSTAs), such as the aldol,[2] Mannich,[3] Michael,[4] and Diels−Alder reactions.[5] In contrast,

(1) (a) For examples, see: Smith, M. B.; March, J. *Advanced Organic Chemistry*, 5th ed.; John Wiley: New York, 2001; p 569. (b) Vollhardt, K. P. C.; Schore, N. E. *Organic Chemistry*, 3rd ed.; Freeman: New York, 1999; p 1039. (c) Clayden, J.; Greeves, N.; Warren, S.; Wothers, P. *Organic Chemistry*; Oxford: New York, 2001; p 726. (d) Kürti, L.; Czakó, B. *Strategic Applications of Named Reactions in Organic Synthesis*; Elsevier: Burlington, 2005; p 86 and p 138. (e) Manyik, R. M.; Frostick, F. C.; Sanderson, J. J.; Hauser, C. R. *J. Am. Chem. Soc.* **1953**, *75*, 5030. (f) Mao, C. L.; Frostick, F. C.; Man, E. H.; Manyik, R. M.; Wells, R. L.; Hauser, C. R. *J. Org. Chem.* **1969**, *34*, 1425. (g) House, H.; Auerbach, R. A.; Gall, M.; Peet, N. P. *J. Org. Chem.* **1973**, *38*, 514. (h) Beck, A. K.; Hoekstra, M. S.; Seebach, D. *Tetrahedron Lett.* **1977**, *13*, 1187. (i) Howard, A. S.; Meerholz, C. A.; Michael, J. P. *Tetrahedron Lett.* **1979**, *15*, 1339. (j) Fleming, I.; Iqbal, J.; Krebs, E.-P. *Tetrahedron* **1983**, *39*, 841. (k) Stefaniak, M. H. *Synlett* **1997**, 677.

(2) (a) Mukaiyama, T.; Narasaka, K.; Banno, K. *Chem. Lett.* **1973**, 1011. (b) Mukaiyama, T.; Narasaka, K.; Banno, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503. (c) Langer, P.; Koehler, V. *Org. Lett.* **2000**, *2*, 1597. (d) Matsukawa, S.; Okano, N.; Imamoto, T. *Tetrahedron Lett.* **2000**, *41*, 103. (e) Delas, C.; Blacque, O.; Moise, C. *Tetrahedron Lett.* **2000**, *41*, 8269. (f) Ishihara, K.; Kondo, S.; Yamamoto, H. *J. Org. Chem.* **2000**, *65*, 9125. (g) Kumareswaran, R.; Reddy, B. G.; Vankar, Y. D. *Tetrahedron Lett.* **2000**, *41*, 8269. (h) Armstrong, A.; Critchley, T. J.; Gourdel-Martin, M.-E.; Kelsey, R. D.; Mortlock, A. A. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1344. (i) Clézio, I. L.; Escudier, J.-M.; Vigroux, A. *Org. Lett.* **2003**, *5*, 161. (j) Ishihara, K.; Yamamoto, H. Boron and Silicon Lewis Acids for Mukaiyama Aldol Reactions. In *Modern Aldol Reactions*; Mahrwald, R., Ed.; 2004; p 25. (k) Mukaiyama, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 5590. (l) Li, H.-J.; Tian, H.-Y.; Wu, Y.-C.; Chen, Y.-J.; Liu, L.; Wang, D.; Li, C.-J. *Adv. Synth. Catal.* **2005**, *347*, 1247. (m) Adhikari, S.; Caille, S.; Hanbauer, M.; Ngo, V. X.; Overman, L. E. *Org. Lett.* **2005**, *7*, 2795. (n) Acocella, M. R.; Massa, A.; Palombi, L.; Villano, R.; Scettri, A. *Tetrahedron Lett.* **2005**, *46*, 6141.

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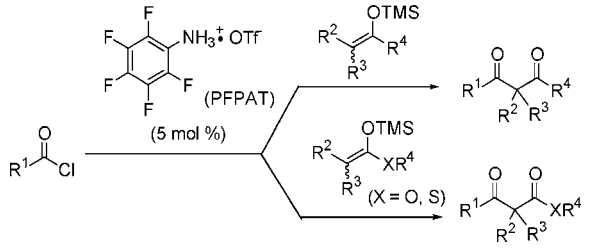
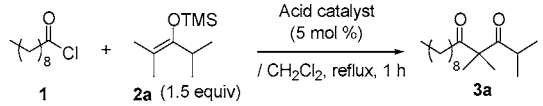
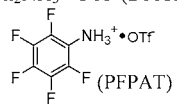
Scheme 1. PFPAT-Catalyzed C-Acylation of Silyl Enolates



there are very few reported methods for the relevant catalytic C-acylation using enol silyl ethers and KSAs or KSTAs

Table 1. Screening of Acid Catalysts



Entry	Acid catalysts	Yield / %[a]
1	None	Trace
2	H_2SO_4	Trace
3	CSA	Trace
4	PPTS	Trace
5	TMSOTf	58
6	$Ph_2NH_3^+$•OTf$^-$ (DPAT)	88
7		92

[a] Determined by ^{1}H NMR.

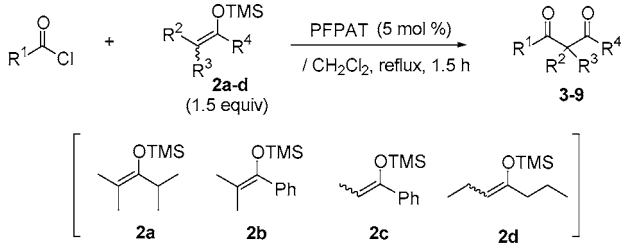
(crossed Claisen-type condensations). Dubac and co-workers reported the first catalytic C-acylation of enol silyl ethers with AcCl promoted by $BiCl_3-3NaI$.[6] This method is not general, however, because it is limited to C-acetylation.

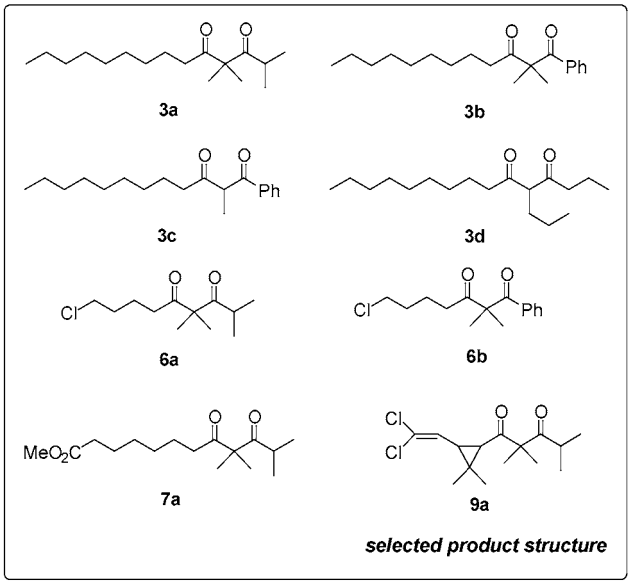
(3) (a) Akiyama, T.; Itoh, J.; Fuchibe, K. *Synlett* **2002**, 1269. (b) Loh, T.-P.; Chen, S.-L. *Org. Lett*. **2002**, *4*, 3647. (c) Jacobsen, M. F.; Skrydstrup, T. *J. Org. Chem.* **2003**, *68*, 7112. (d) Loncaric, C.; Manabe, K.; Kobayashi, S. *Adv. Synth. Catal.* **2003**, *345*, 1187. (e) Takahashi, E.; Fujisawa, H.; Mukaiyama, T. *Chem. Lett*. **2004**, *33*, 936. (f) Hamada, T.; Manabe, K.; Kobayashi, S. *J. Am. Chem. Soc*. **2004**, *126*, 7768. (g) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem., Int. Ed*. **2004**, *43*, 1566.(h) Akiyama, T.; Matsuda, K.; Fuchibe, K. *Synlett* **2005**, 322. (i) Akiyama, T.; Suzuki, A.; Fuchibe, K. *Synlett* **2005**, 1024. (j) Saruhashi, K.; Kobayashi, S. *J. Am. Chem. Soc.* **2006**, *128*, 11232. Other references cited therein.

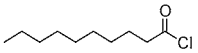
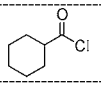
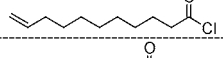
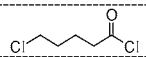
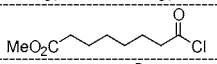
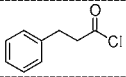
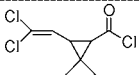
(4) (a) Gnaneshwar, R.; Wadgaonkar, P. P.; Silvaram, S. *Tetrahedron Lett.* **2003**, *44*, 6047. (b) Wang, X.; Adachi, M.; Iwai, H.; Takatsuki, H.; Fujita, K.; Kubo, M.; Oku, A.; Harada, T. *J. Org. Chem*. **2003**, *68*, 10046. (c) Jaber, N.; Assie, M.; Fiaud, J.-C.; Collin, J. *Tetrahedron* **2004**, *60*, 3075. (d) Shen, Z.-L.; Ji, S.-J.; Loh, T.-P. *Tetrahedron Lett.* **2005**, *46*, 507. (e) Wang, W.; Li, H.; Wang, J. *Org. Lett.* **2005**, *7*, 1637.

(5) (a) Danishefsky, S.; Kitahara, T. *J. Am. Chem. Soc*. **1974**, *96*, 7807. (b) Danishefsky, S. *Acc. Chem. Res*. **1981**, *14*, 400. (c) Danishefsky, S. J.; Daninno, M. P. *Angew. Chem., Int. Ed. Engl*. **1987**, *26*, 15. (d) Herczzegh, P.; Kovacs, I.; Erdosi, G.; Varge, T.; Agocs, A.; Szilagyi, L.; Sztaricskai, F.; Berecibar, A.; Lukacs, G.; Olesker, A. *Pure Appl. Chem*. **1997**, *69*, 519. (e) Kozmin, S. A.; Rawal, V. H. *J. Org. Chem*. **1997**, *62*, 5252. (f) Kozmin, S. A.; Janey, J. M.; Rawal, V. H. *J. Org. Chem*. **1999**, *64*, 3039. (g) Simonsen, K. B.; Svenstrup, N.; Roberson, M.; Jorgensen, K. A. *Chem.—Eur. J*. **2000**, *6*, 123. (h) Amii, H.; Kobayashi, T.; Terasawa, H.; Uneyama, K. *Org. Lett*. **2001**, *3*, 3103. (i) Inokuchi, T.; Okano, M.; Miyamoto, T. *J. Org. Chem*. **2001**, *66*, 8059. (j) Motoyama, Y.; Koga, Y.; Nishiyama, H. *Tetrahedron* **2001**, *57*, 853. (k) Spino, C.; Rezaei, H.; Dory, Y. L. *J. Org. Chem*. **2004**, *69*, 757.

Table 2. C-Acylation of Enol Silyl Ethers **2** with Acid Chlorides Using the PFPAT Catalyst





Entry	Acid chloride	Enol silyl ether	Product	Yield / %[a]
1		**2a**	**3a**	91
2		**2b**	**3b**	80
3		**2c**	**3c**	62
4		**2d**	**3d**	70
5		**2a**	**4a**	70
6		**2a**	**5a**	82
7		**2b**	**5b**	80
8		**2a**	**6a**	90
9		**2b**	**6b**	85
10		**2a**	**7a**	84
11		**2a**	**8a**	92
12		**2a**	**9a**	85

[a] Isolated.

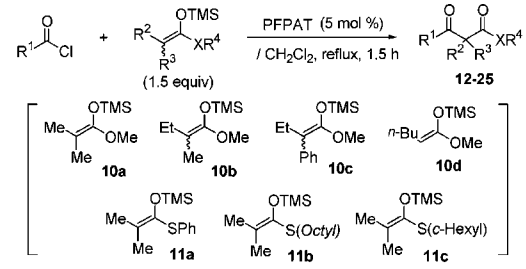
Recently, catalytic enantioselective C-acylation of KSAs with acid anhydrides was developed by Fu and co-workers.[7]

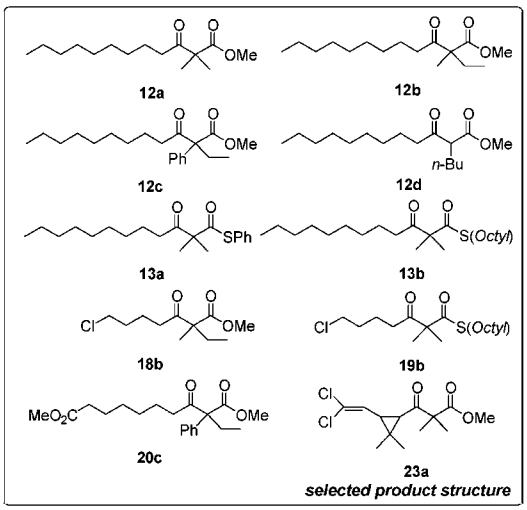
In connection with our continuing studies on the development of Ti (*or* Zr) Claisen condensation[8] and related

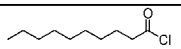
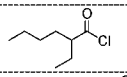
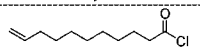
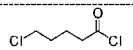
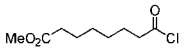
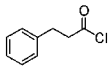
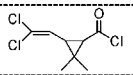
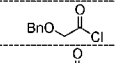
(6) Roux, C. L.; Mandrou, S.; Dubac, J. *J. Org. Chem*. **1996**, *61*, 3885.

(7) (a) Mermerian, A. H.; Fu, G. C. *J. Am. Chem. Soc*. **2003**, *125*, 4050. (b) Mermerian, A. H.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 5604.

Table 3. PFPAT-Catalyzed C-Acylation between KSAs **10** or KSTAs **11** and Acid Chlorides

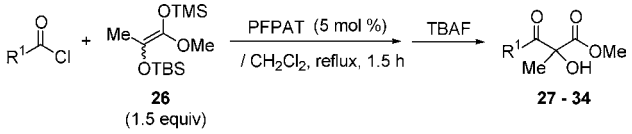


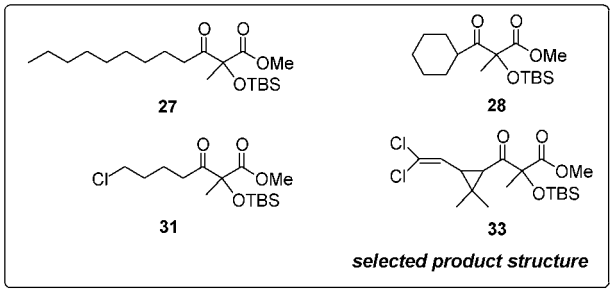


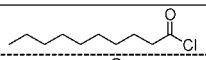
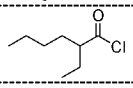
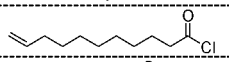
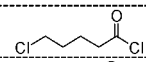
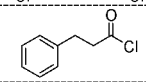
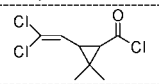
Entry	Acid chloride	KSA or KSTA	Product	Yield / %[a]
1		**10a**	**12a**	92
2		**10b**	**12b**	87
3		**10c**	**12c**	86
4		**10d**	**12d**	80[b]
5		**11a**	**13a**	60[b]
6		**11b**	**13b**	80[b]
7		**11c**	**13c**	72[b]
8		**10a**	**14a**	84
9		**10b**	**14b**	84
10		**10c**	**14c**	66
11		**10a**	**15a**	74 (trace)[c]
12		**10a**	**16a**	91
13		**10b**	**16b**	84
14		**10c**	**16c**	80
15		**10d**	**16d**	76[b]
16		**11c**	**17c**	69[b]
17		**10a**	**18a**	76
18		**10b**	**18b**	85
19		**10c**	**18c**	77
20		**11b**	**19b**	71[b]
21		**10a**	**20a**	92
22		**10c**	**20c**	79
23		**10a**	**21a**	76
24		**10c**	**21c**	79
25		**10d**	**21d**	89[b]
26		**11a**	**22a**	65[b]
27		**10a**	**23a**	91
28		**10c**	**23c**	80
29		**10a**	**24a**	63
30		**10a**	**25a**	79

[a] Isolated. [b] 2.0 equiv of KSA or KSTA was used. [c] NaOH-catalyzed method using the corresponding methyl ester.

Table 4. PFPAT-Catalyzed C-Acylation of KSA **26** with Acid Chlorides





Entry	Acid chloride	Product	Yield / %[a]
1		**27**	88
2		**28**	88
3		**29**	78
4		**30**	74
5		**31**	75
6		**32**	87
7		**33**	74
8		**34**	65

[a] Isolated.

reactions,[9] we present here a mild and efficient pentafluorophenylammonium triflate (PFPAT)[10a] catalyzed C-acylation between enol silyl ethers **2a**−**d** and acid chlorides (Scheme 1). The present protocol was successfully extended to a

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closely related C-acylation of KSAs **10a**−**d**, **26**, or KSTAs **11a**,**b** with acid chlorides.

The initial attempt was guided by the reaction between decanoyl chloride **1** and enol silyl ether **2a** (1.5 equiv) using several acid catalysts (Table 1). The major problem of metal-catalyzed C-acylation using enol silyl ethers lies in the difficulty in controlling competitive O-acylation. Acid organocatalysts (5 mol %) were screened to overcome this problem. Conventional Brønsted acids (H_2SO_4, CSA) and PPTS resulted in no reaction (entries 2−4). Although TMSOTf is a representative Lewis acid catalyst for the Mukaiyama aldol and Michael reactions, more stable and easy to handle solid ammonium triflate catalysts such as diphenylammonium triflate (DPAT)[10b] and PFPAT[10a] had unexpectedly apparent higher reactivity than TMSOTf (entries 6 and 7). In addition, undesirable O-acylation was completely suppressed. Thus, we chose the PFPAT catalyst for the present method.

Table 2 lists the successful results of the present PFPAT-catalyzed C-acylation using a variety of enol silyl ethers **2a**−**d** and acid chlorides under optimized conditions. Various β-diketones were obtained in good to excellent yield. Several functionalities in acid chloride, such as a terminal double bond, a δ-chloro, a methyl ester, and a cyclopropane, were tolerated (entries 6−12).

Next, we investigated PFPAT-catalyzed C-acylation, i.e., Claisen-type condensation between KSAs **10a**−**d** or KSTAs **11a**−**c** and acid chlorides. Table 3 lists the successful results. The salient features are as follows. (i) Although stereocongested electrophiles tend to resist Claisen condensation, less reactive branched as well as reactive linear acid chlorides smoothly underwent the present reaction to give the corresponding β-keto esters in good to excellent yield (30 examples; 60−92%). (ii) Traditional C-acylation cannot be applied to α,α-dialkylated ester derivatives because the retro-Claisen condensation generally predominates.[1] The present method was powerful enough to provide a variety of α,α-dialkylated β-keto esters and thioesters. (iii) The reaction using KSA **10b**,**c** bearing ethyl and/or phenyl groups in the α,α-positions proceeded smoothly to give the desired highly stereocongested β-keto esters in good yield. (iv) Compared with NaOH-catalyzed Claisen condensation,[9d] the present method had much higher reactivity (entry 11). In addition, KSA equivalents were significantly reduced to 1.5−2.0, whereas the NaOH-catalyzed method required ca. 3.0 equiv. (v) Several functionalities in the acid chloride were tolerated under the reaction conditions. By way of contrast, methyl esters were not compatible with the NaOH-catalyzed method (entries 21 and 22).[9d] (vi) KTSAs **11a**−**c** underwent the desired reaction to give the desired β-keto thioesters.

The reaction between KSA **26**, derived from methyl lactate, and acid chlorides was investigated (Table 4). Despite the utility of the α-oxy functionalized product, neither NaOH-catalyzed nor powerful Ti Claisen condensations can be applied to **26** (no reaction). Similar to the reaction using KSAs **10a**−**d**, a variety of α-hydroxy-β-keto esters were successfully obtained in good to excellent yield (8 examples; 65−88%).

In conclusion, we have developed a regioselective C-acylation of both enol silyl ethers and KSAs (or KSTAs) with acid chlorides, promoted by the PFPAT catalyst (total of 50 examples). The present mild and general method is a new avenue for the synthesis of a variety of β-diketones and β-keto esters.

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Supporting Information Available: The experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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