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Concise Report

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Synthesis of *trans*-2-(Disubstituted-amino)alkenyl Polyoxyperfluoroalkyl Ketones from Tertiary Amines and Perfluoroalkyl Ether Carboxylates Featuring "–CF_2O–" Units†

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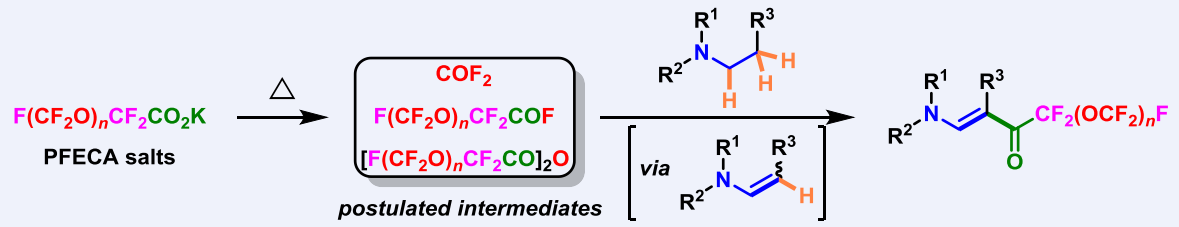
Keywords

Fluorine | Oxidation | Acylation | Perfluoroalkyl ether carboxylates | Tertiary amines | Enaminones

Comprehensive Summary



- **Bench-stable, industrially available reagents**
- **Multiple functionalizations in one pot**
- **Convenient to operate**
- **28 examples**
- **Simple purification**
- **Up to 84% yield**

A one-pot transformation of aliphatic and aromatic tertiary amines to novel fluorinated enaminones has been developed, utilizing perfluoroalkyl ether carboxylates (PFECA salts) featuring "–CF_2O–" units as the fluorine-containing reagents. Carbonyl fluoride, acyl fluorides and anhydrides by thermal decomposition of these PFECA salts were proposed to act as key active species that trigger the tandem oxidation–acylation process of tertiary amines, through enamine intermediates.

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Background and Originality Content

β-Amino-*α*,*β*-unsaturated carbonyl compounds (enaminones) are a class of vinylogous amides that serve as versatile building blocks in organic synthesis, especially for the construction of a wide range of heterocyclic compounds.[1] To date, the utility of enaminones as biologically active compounds or their precursors,[1k-m,2] ligands for transition metal catalysis,[3] and organocatalysts[4] has also been extensively exploited. Several useful synthetic approaches to enaminones include treatment of *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA),[5] Bredereck's reagent,[6] or Gold's reagent[7] with ketones, as well as the reaction of primary or secondary amines with *α*,*β*-unsaturated carbonyl compounds bearing a *β*-leaving group by addition–elimination pathways.[8] Recently, some novel synthetic methodologies have also emerged for the construction of fluorinated enaminones.[9]

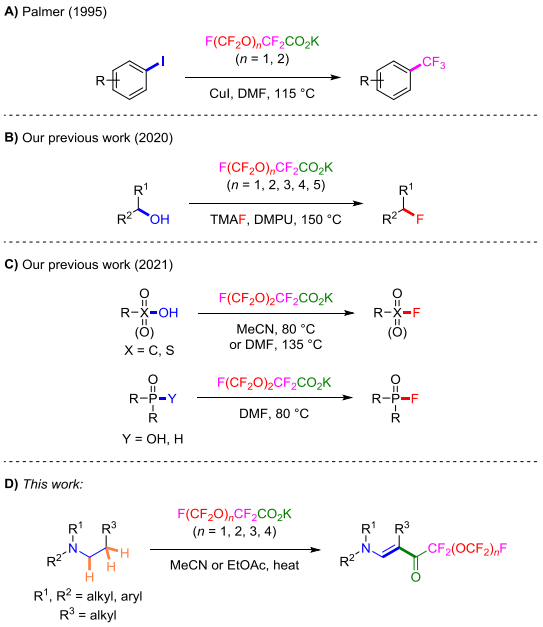
In addition to the aforementioned methods, the oxidation–acylation for the facile conversion of tertiary amines to enaminones in a *stepwise* fashion has also been reported, albeit to a much lesser extent. To this end, one strategy involves *in situ* dehydrogenation of amines to give enamines using oxidants such as $TiCl_4$[10] or $(^tBuO)_2/CuBr_2$,[11] followed by subsequent acylation reactions. When highly electron-deficient acyl precursors are employed such as perchloroacyl chlorides,[12] perfluoro(chloro)acyl fluorides,[12a] trifluoroacetic anhydride,[13] perfluoroalkyl halides,[14] hexachloroacetone,[15] or phosgene,[16] they may function as *both* one-electron oxidizing agents *and* acylating agents to accomplish the formation of perfluoro(chloro)acyl-based enaminones. The reactions were commonly believed to proceed *via* single electron transfer (SET) pathways. However, the low boiling points, high reactivity and toxicity of these perhalogenated reagents, along with their limited availability and narrow substrate scope have always been retarding research on the intriguing enaminone synthesis reactions.

Perfluoroalkyl ether carboxylic acids (PFECAs), with the general formula of $F(CF_2O)_nCF_2CO_2H$, are industrial by-products in the manufacture of hexafluoropropene oxide (HFPO).[17] In comparison to the non-oxygenated counterparts, *i.e.*, perfluoroalkyl carboxylic acids (PFCAs), one of the most prominent features of the PFECAs is the fluoroether chain with consecutive "$–CF_2O–$" modules. This structural characteristic makes them prone to be fully fragmented upon decarboxylation. The higher degradability[18] and lower toxicity[19] of the short-chain PFECAs are making them potential alternatives to persistent organic pollutants (POPs) for design of more ecofriendly fluorosurfactants and functional materials.[20]

The synthetic methodology utilizing $F(CF_2O)_nCF_2CO_2M$ to introduce fluorine-containing functional groups has also been developed (Scheme 1). In 1995, Palmer *et al*.[21] reported the use of $CF_3OCF_2CO_2K$ and $F(CF_2O)_2CF_2CO_2K$ in copper(I)-mediated trifluoromethylation of aryl or benzyl halides (Scheme 1A). Recently, such PFECA salts have also been developed by us as carbonyl fluoride precursors for the deoxyfluorination of alcohols,[22] carboxylic acids, sulfonic acids, phosphinic acids and secondary phosphine oxides[23] (Scheme 1B–C). The thermal decomposition of this kind of perfluoroetherated carboxylates is expected to produce carbon dioxide, a trifluoromethide species ("KCF_3" for example) and varying amount of carbonyl fluoride, depending on the chain length. Thus, these salts can serve as latent multifunctional reagents for introduction of manifold fluorine-containing groups by reaction design.

Since (polyoxy)perfluoroacyl fluorides and anhydrides are unstable, low-boiling-point and highly toxic reagents, we aim to use safer reagents to investigate the analogous reaction towards tertiary amines. Fortunately, $F(CF_2O)_nCF_2CO_2M$ may combine carbonyl fluoride with untransformed carboxylates to produce the fluorinated electrophiles *in situ* by controlling the decomposition rates and pathways of $F(CF_2O)_nCF_2CO_2M$. These PFECA salts can be readily prepared from corresponding esters by hydrolysis with metal hydroxides [M = alkaline (earth) metal] or quaternization of tertiary amines [M = NR_4]. They are bench-stable, storable and easy-to-handle reagents, prospective to be a novel source of perfluoroether-modified enaminone precursors in the presence of tertiary amines. Herein, we report the reaction between tertiary amines and $F(CF_2O)_nCF_2CO_2K$, which enables the synthesis of multifunctionalized 3-(disubstituted-amino)alkenyl polyoxyperfluoroalkyl ketones through a remarkably straightforward approach (Scheme 1D).

Scheme 1 Reactions of $F(CF_2O)_nCF_2CO_2M$

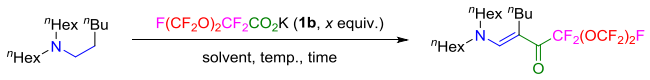


Results and Discussion

Inasmuch as PFO2HxA salts [$F(CF_2O)_2CF_2CO_2M$] are proven to be effective carbonyl fluoride precursors,[22-23] the potassium salt of PFO2HxA (**1b**, PFO2HxA-K) was chosen to begin our screening of the reaction conditions. With tri-*n*-hexylamine (**2a**) as the substrate, enaminone **3b** could be afforded in moderate yield when ethyl acetate (Table 1, entry 1), glymes (Table 1, entries 2, 3) or acetonitrile (Table 1, entry 4) was used as solvents, where acetonitrile gave the best result of 50% yield (Table 1, entry 4). In contrast, other polar aprotic solvents such as DMF or DMSO appeared to be unsuitable for the reaction (Table 1, entries 5, 6), presumably due to their higher reactivity towards carbonyl fluoride.[24] Other non-polar solvents, *e.g.*, 1,4-dioxane, DCE, and toluene, did not provide satisfactory results, either (Table 1, entry 7–9), which might be attributed to the poor coordination ability of the solvent to separate bare carboxylate ions from potassium ions, inhibiting the decarboxylation processes. Insufficiency of **1b** was a detriment to the yield (Table 1, entry 10). In contrast, a higher yield was obtained by employing 2.0 equiv. of **1b** (Table 1, entry 11), and little did such equivalent affect the result when excess (Table 1, entry 4, 12–14). Additionally, the concentration of substrates was found to be a crucial factor in the reaction (Table 1, entries 11, 15–17). With *ca.* 1.6 moles of **1b** dissolved in per liter acetonitrile, the yield reached up to 66% (Table 1, entry 16). Besides, it is appealing that the reaction seemed to be insensitive to air, at the expense of a minor yield loss (Table 1, entry 18). A reaction temperature of 85 °C rendered the yield slightly higher (Table 1, entry 19), whereas the decomposition rate of **1b** turned strikingly slow below 70 °C (Table 1, entries 21, 22). Furthermore, a reaction period of 6 h was perceived to suffice, giving a 70% yield

(Table 1, entry 25), and an extension of reaction time did not significantly impact the result (Table 1, entries 19, 26).

Table 1 Optimization of the reaction conditions on PFO2HxA-K[a]



2a 3b

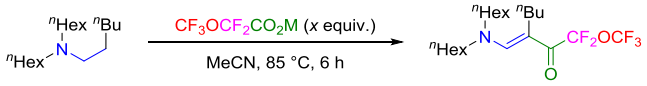
entry	*x*/equiv.	solvent (mL)	temp./°C	time/h	yield[b]/%
1	3.0	EtOAc (1.5)	80	12	42
2	3.0	monoglyme (1.5)	80	12	48
3	3.0	diglyme (1.5)	80	12	19
4	3.0	MeCN (1.5)	80	12	50
5	3.0	DMF (1.5)	80	12	5
6	3.0	DMSO (1.5)	80	12	0
7	3.0	1,4-dioxane (1.5)	80	12	0
8	3.0	DCE (1.5)	80	12	7
9	3.0	toluene (1.5)	80	12	0
10	1.5	MeCN (1.5)	80	12	43
11	2.0	MeCN (1.5)	80	12	57
12	2.5	MeCN (1.5)	80	12	52
13	3.5	MeCN (1.5)	80	12	51
14	4.0	MeCN (1.5)	80	12	50
15	2.0	MeCN (1.0)	80	12	55
16	2.0	MeCN (0.5)	80	12	66
17	2.0	MeCN (0.25)	80	12	42
18[c]	2.0	MeCN (0.5)	80	12	60
19	2.0	MeCN (0.5)	85	12	68
20	2.0	MeCN (0.5)	75	12	66
21	2.0	MeCN (0.5)	70	12	10
22	2.0	MeCN (0.5)	65	12	< 1
23	2.0	MeCN (0.5)	85	1.5	11
24	2.0	MeCN (0.5)	85	3	59
25	2.0	MeCN (0.5)	85	6	70 (60[d])
26	2.0	MeCN (0.5)	85	24	68

[a] Reaction conditions: tri-*n*-hexylamine (**2a**, 0.4 mmol, 1.0 equiv.) and PFO2HxA-K (**1b**, as indicated) were reacted in anhydrous solvent under an argon atmosphere. [b] The yield of **3b** was determined by ^{19}F NMR of the crude reaction mixture using benzotrifluoride as the internal standard. [c] The reaction was conducted in air. [d] Isolated yield.

Clearly, the optimized conditions with respect to PFO2Hx-K might not be the most suitable ones for other homologous PFECA salts, especially in terms of their equivalents and concentrations. It can be foreseen that perfluoro-2-methoxyacetates (PFMOAA-M, $CF_3OCF_2CO_2M$) are much less efficient to furnish the desired products as they behave less like carbonyl fluoride reservoirs. In addition, the fate of the concomitantly generated though postulated "trifluoromethyl anion", which is apt to complicate the reaction, is still unclear. Thus, a series of PFMOAA salts with diversified cations was prepared to apply to the reaction for not only better results but illustration on the function of cations as well (Table 2).

To draw an analogy with the best screened conditions of PFO2Hx-K above, PFMOAA-M was initially set at 3.0 equiv. relative to **2a** (1.0 equiv. for construction of acyl moiety in enaminone **3** and 2.0 equiv. for release of COF_2) in a 1.6 M solution of acetonitrile (*i.e.*, 0.75 mL MeCN). For PFMOAA salts with "harder" cations (*e.g.*, Na^+, Ca^{2+}, Sr^{2+} and Ba^{2+}) as counterions, the desired product could not be obtained presumably due to the strong electrostatic interactions between ions that inhibited decarboxylation processes of such salts (Table 2, entry 1, 6–8). Quaternary ammonium salts almost completely decomposed under the reaction conditions, yet leading to other complex decomposition products remaining **2a** nearly intact (Table 2, entries 9, 10). The ^{19}F NMR pattern for reaction using PFMOAA-Cs as substrate resembled that of PFMOAA-NMe_4, though unreacted PFMOAA-Cs and a small amount of **3a** were also detected (Table 2, entry 4). Amongst all of the PFMOAA salts, only potassium and rubidium salts were verified to be effective reagents for the reaction, with PFMOAA-K exhibiting the highest yield (Table 2, entries 2, 3). Furthermore, the reaction was completely inhibited by the chelating agent 18-crown-6 (Table 2, entry 5), suggesting that solvated potassium ions are of critical importance to accessing enaminone **3a**.

Table 2 Optimization of the reaction conditions on PFMOAA-M[a]



2a 3a

entry	PFMOAA-M	*x* (equiv.)	solvent (mL)	yield[b]/%
1	$CF_3OCF_2CO_2Na$	3.0	MeCN (0.75)	0
2	$CF_3OCF_2CO_2K$	3.0	MeCN (0.75)	40 (33[d])
3	$CF_3OCF_2CO_2Rb$	3.0	MeCN (0.75)	18
4	$CF_3OCF_2CO_2Cs$	3.0	MeCN (0.75)	2
5[c]	$CF_3OCF_2CO_2$[K(18-crown-6)]	3.0	MeCN (0.75)	0
6	$(CF_3OCF_2CO_2)_2Ca$	1.5	MeCN (0.75)	0
7	$(CF_3OCF_2CO_2)_2Sr$	1.5	MeCN (0.75)	0
8	$(CF_3OCF_2CO_2)_2Ba$	1.5	MeCN (0.75)	0
9	$CF_3OCF_2CO_2^-$ Me_4N^+	3.0	MeCN (0.75)	0
10	$CF_3OCF_2CO_2^-$ $Me_3N^+(^nC_{18}H_{37})$	3.0	MeCN (0.75)	0
11	$CF_3OCF_2CO_2K$	3.5	MeCN (0.75)	26
12	$CF_3OCF_2CO_2K$	3.5	MeCN (1.0)	31
13	$CF_3OCF_2CO_2K$	3.0	MeCN (0.5)	24
14	$CF_3OCF_2CO_2K$	3.0	MeCN (1.0)	32
15	$CF_3OCF_2CO_2K$	2.5	MeCN (0.5)	35
16	$CF_3OCF_2CO_2K$	2.5	MeCN (0.75)	33
17	$CF_3OCF_2CO_2K$	2.5	MeCN (1.0)	33

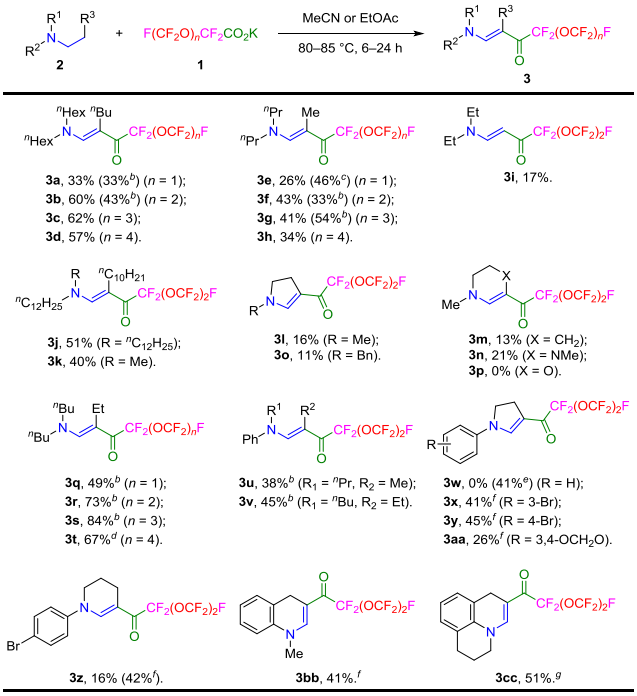
[a] Reaction conditions: tri-*n*-hexylamine (**2a**, 0.4 mmol, 1.0 equiv.) and PFMOAA-M (as indicated) were reacted in anhydrous acetonitrile (0.75 mL) at 85 °C for 6 h under an argon atmosphere. [b] The yield of **3a** was determined by ^{19}F NMR of the crude reaction mixture using benzotrifluoride as the internal standard. [c] PFMOAA-K (3.0 equiv.) and 18-crown-6 (3.0 equiv.) were applied. [d] Isolated yield.

The optimal reaction conditions for PFMOAA-K speculated from those of PFO2HxA-K [1.0 equiv. for acylation plus (2.0/*n*) equiv. of latent "COF_2" excess for $F(CF_2O)_nCF_2CO_2K$ whose concentration was kept 1.6 M in acetonitrile, as mentioned above] were validated by additional control experiments (Table 2, entries 11–17). With the rule of thumb concluded thereby, it was deduced that 1.7 equiv. PFO3OA-K in 0.45 mL acetonitrile and 1.5 equiv. PFO4DA-K in 0.4 mL acetonitrile were the respective appropriate conditions when 0.4 mmol tertiary amine substrate was applied. Besides, it is noteworthy that **2a** converted more to its difluorocarbene-derived side product $^nHex_3N^+CF_2H$ as postulated by ^{19}F NMR (δ_F = −112.06, d, J = 57.8 Hz, in MeCN) with PFMOAA-K (33%) compared to PFO2HxA-K (10%) under their respective best conditions, which might result in a much lower yield of **3a** than **3b**.

With the optimized conditions in hand, we next started to in-

vestigate the scope of substrates (Scheme 2). In terms of other $F(CF_2O)_nCF_2CO_2K$ reagents, longer-chain homologs PFO3OA-K (**1c**, n = 3) and PFO4DA-K (**1d**, n = 4) performed fairly well in comparison with PFO2HxA-K (**3b–3d**, **3f–3h**). PFMOAA-K, on the other hand, did not yield equally desirable results under similar conditions (**3a**, **3e**). With **1b** applied, tri-*n*-alkylamines with longer chains gave satisfactory results (**3b**, **3j**), whereas the yields of corresponding enaminones decreased sharply with amines becoming less sterically demanding (**3f**, **3i**). We postulate that side reactions involving difluorocarbene and carbonyl fluoride towards less sterically encumbered substrates may become more prominent, leading to lower yields of target enaminone products. The *trans*-configuration of enaminone **3f** could be confirmed by its 2D NOESY spectrum (see Supporting Information). A single methyl substituent on nitrogen did not affect the yield to a great extent with an amine bearing two other dodecyl groups (**3k**). In contrast, methyl- or benzyl-substituted cyclic aliphatic amines are more prone to undergo side reactions, leading to lower yields of enaminones (**3l–3o**), and oxidation-reluctant *N*-methylmorpholine is seemingly incompatible with the reaction conditions (**3p**).

Scheme 2 Reaction scope for the synthesis of enaminones with aliphatic amines[a]

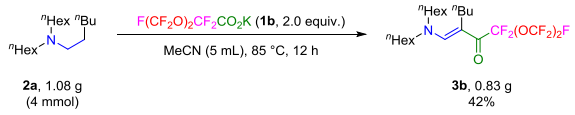


[a] Reaction conditions: **2** (0.4 mmol, 1.0 equiv.) and **1** (**1a**, 3.0 equiv.; **1b**, 2.0 equiv.; **1c**, 1.7 equiv.; **1d**, 1.5 equiv.) were reacted in anhydrous acetonitrile (**1a**, 0.75 mL; **1b**, 0.5 mL; **1c**, 0.45 mL; **1d**, 0.4 mL) at 85 °C for 6 h under an argon atmosphere. [b] Reaction conditions: **2** (0.4 mmol, 1.0 equiv.) and **1** (3.0 equiv.) were reacted in anhydrous ethyl acetate (1.5 mL) at 80 °C for 24 h under a nitrogen atmosphere. [c] Reaction conditions: **2** (0.2 mmol, 1.0 equiv.) and **1a** (6.0 equiv.) were reacted in anhydrous ethyl acetate (1.5 mL) at 80 °C for 24 h under an argon atmosphere. [d] Reaction conditions: **2** (0.4 mmol, 1.0 equiv.) and **1d** (3.0 equiv.) were reacted in anhydrous ethyl acetate (2.0 mL) at 80 °C for 24 h under a nitrogen atmosphere. [e] Reaction conditions: **2** (0.3 mmol, 1.0 equiv.) and **1b** (3.0 equiv.) were reacted in anhydrous ethyl acetate (1.5 mL) at 80 °C for 24 h under a nitrogen atmosphere. [f] Reaction conditions: **2** (0.6 mmol, 1.0 equiv.) and **1b** (3.0 equiv.) were reacted in anhydrous ethyl acetate (3.0 mL) at 80 °C for 24 h under a nitrogen atmosphere. [g] Reaction conditions: **2** (0.2 mmol, 1.0 equiv.) and **1b** (3.0 equiv.) were reacted in anhydrous ethyl acetate (1.0 mL) at 80 °C for 24 h under a nitrogen atmosphere.

Furthermore, aromatic tertiary amines were also taken into account. Under the same reaction conditions in regard to PFO2HxA-K in acetonitrile, we found that electron-rich aromatic tertiary amines like *N*-phenylpyrrolidine (**2w**) are more susceptible to side reactions such as Friedel–Crafts acylation, while *N*-(4-bromophenyl)piperidine turned out to be much less reactive possibly attributed to its electron-deficiency and limited solubility (**3z**). Hence, a less polar solvent, ethyl acetate, was utilized instead. In addition, a larger amount of **1b** (3.0 equiv.) and prolonged reaction duration (24 h) were applied to offset the lowered reactivity of aromatic amines and ensure a better degree of completion of the reaction. Under the modified conditions, phenyl-substituted acyclic or cyclic amines performed comparably well to furnish the desired enaminone products (**3u–3w**), and the presence of a bromo substituent did not substantially affect the yields (**3x–3z**). An electron-rich (1,3-benzodioxolyl)pyrrolidine derivative was able to undergo the anticipated reaction but in a lower yield (**3aa**). Ring-fused heterocycles, such as 1-methyl-1,2,3,4-tetrahydroquinoline and julolidine, are also suitable starting materials to provide the corresponding products in reasonable yields (**3bb**, **3cc**). With ethyl acetate employed, aliphatic tri-*n*-hexylamine and tri-*n*-propylamine could still convert into the desired products in similar yields (**3a**, **3b**, **3e–3g**), and it was verified to be an excellent solvent using tri-*n*-butylamine as the substrate (**3q–3t**).

The synthetic utility of the reaction was confirmed by the large-scale preparation of **3b** (Scheme 3). The reaction proceeded well with 4 mmol tri-*n*-hexylamine applied, though in a slightly lower yield compared with the 0.4 mmol scale reaction.

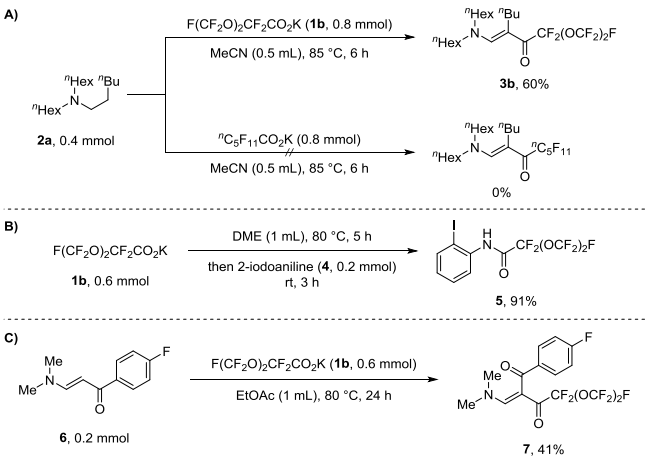
Scheme 3 Scale-up reaction[a]



[a] Reaction conditions: tri-*n*-hexylamine (**2a**, 4.0 mmol, 1.0 equiv.) and PFO2HxA-K (**1b**, 8.0 mmol, 2.0 equiv.) were reacted in anhydrous acetonitrile (5 mL) at 85 °C for 12 h under an argon atmosphere.

In our published paper,[22] we have demonstrated the generation of highly reactive carbonyl fluoride based on the decomposition of $F(CF_2O)_nCF_2CO_2M$. Notwithstanding, it is far less sufficient to unravel the reaction pathways with respect to tertiary amines. To gain a better understanding of the mechanism, a series of control experiments were carried out (Scheme 4). When potassium perfluorohexanoate (PFHxA-K) was used instead of PFO2HxA-K (Scheme 4A), no apparent decomposition was observed. This indicates that the PFECA salts are more thermally unstable than PFCA salts, and that the decomposition products might serve as key intermediates in the formation of enaminones. The decomposition products were demonstrated to acylate 2-iodoaniline (**4**) to access the corresponding amide **5**, which suggests the generation

Scheme 4 Control experiments

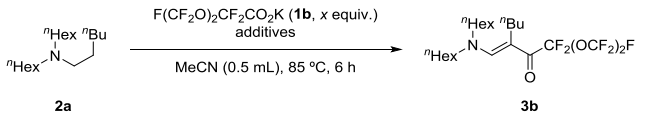


of polyoxyperfluoroacyl fluoride (R_FCOF) or anhydride [$(R_FCO)_2O$] (Scheme 4B). Moreover, less electron-poor enaminone **6** was readily converted into enaminedione **7** in the presence of **1b**, and thus it was postulated enamine moiety as a possible nucleophilic component in terms of product formation (Scheme 4C). In other words, tertiary amines may be initially oxidized to enamines which are further acylated to the corresponding enaminones with respect to the title reaction. The *in situ* generated electrophilic acyl derivatives, including COF_2, acyl fluorides and anhydrides, were regarded as the most plausible oxidants and acylating agents.

The role of acyl derivatives was determined by further mechanistic studies (Table 3). With bis(trichloromethyl) carbonate (BTC) and potassium fluoride applied as additives to simulate the complete decomposition of PFO2HxA-K to the corresponding acylating agents, the desired enaminone product **3b** was observed by ^{19}F NMR monitoring, though in lower yields (Table 3, entries 1–3). By reducing the redundant amount of KF, the presumable acyl fluoride or anhydride alone was still capable of realizing the conversion (Table 3, entries 4, 5) where acyl chloride failed (Table 3, entry 6), revealing that an excess of potassium fluoride may be requisite. Additionally, the partial inhibition of the transformation in the presence of an electron acceptor *m*-dinitrobenzene (*m*-DNB) or a radical scavenger 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) suggests an SET process within (Table 3, entries 1, 7, 8).

Given the above investigations in addition to reported observations,[12a,13a,22-23] a plausible mechanism of the reaction encompassing four main stages was accordingly proposed (Figure 1). In terms of stage I, with the coordination assistance of solvent molecules, the potassium-bound perfluoroalkyl ether carboxylate **1** dissociates its anion **A**, which then decarboxylates to give a fluorinated carbanion **B**. Bearing an excellent perfluoroalkoxy leaving group,[25] **B** can undergo spontaneous cleavage of a series of C–O bonds, yielding difluorocarbene, a varying amount of carbonyl fluoride and trifluoromethoxide **D**. The combination of **D** with potassium ion within **1** gives potassium fluoride that precipitates out from the solution upon aggregation to release another COF_2 molecule. As carbonyl fluoride accumulates, it tends to bind to weakly nucleophilic carboxylate **A** to afford the adduct **E** (Figure 1, stage II). Subsequent inter- or intramolecular fluoride transfer and departure of fluoroformate ion lead to the formation of acyl

Table 3 Mechanistic investigations into the role of acyl derivatives[a]



2a 3b

entry	*x* (equiv.)	additives (equiv.)	yield[b]/%	notes
1	2.00	none	70	$COF_2/R_FCOX + KF + :CF_2$
2[c]	1.33	BTC (0.45) + KF (3.33)	42	$R_FCOF + KF + KCl$
3[c]	1.60	BTC (0.27) + KF (2.00)	52	$(R_FCO)_2O + KF + KCl$
4[d]	1.33	BTC (0.45) + KF (1.33)	30	$R_FCOF + KCl$
5[d]	1.60	BTC (0.27)	28	$(R_FCO)_2O + KCl$
6	1.33	BTC (0.45)	0	$R_FCOCl + KCl$
7	2.00	*m*-DNB (3.00)	48	–
8	2.00	TEMPO (3.00)	45	–

[a] Reaction conditions: tri-*n*-hexylamine (**2a**, 0.4 mmol, 1.0 equiv.), PFO2HxA-K (**1b**, as indicated) and additives (as indicated) were reacted in anhydrous acetonitrile (0.5 mL) at 85 °C for 6 h under an argon atmosphere. [b] The yield of **3b** was determined by ^{19}F NMR of the crude reaction mixture using benzotrifluoride as the internal standard. [c] Stoichiometric amount of **1b**, BTC and spray-dried potassium fluoride were used to have the same amount of acylating agents and KF as that by complete decomposition of PFO2HxA-K in entry 1. [d] Stoichiometric amount of **1b**, BTC and spray-dried potassium fluoride were used to have the same amount of acylating agents but no redundant KF as that by complete decomposition of PFO2HxA-K in entry 1.

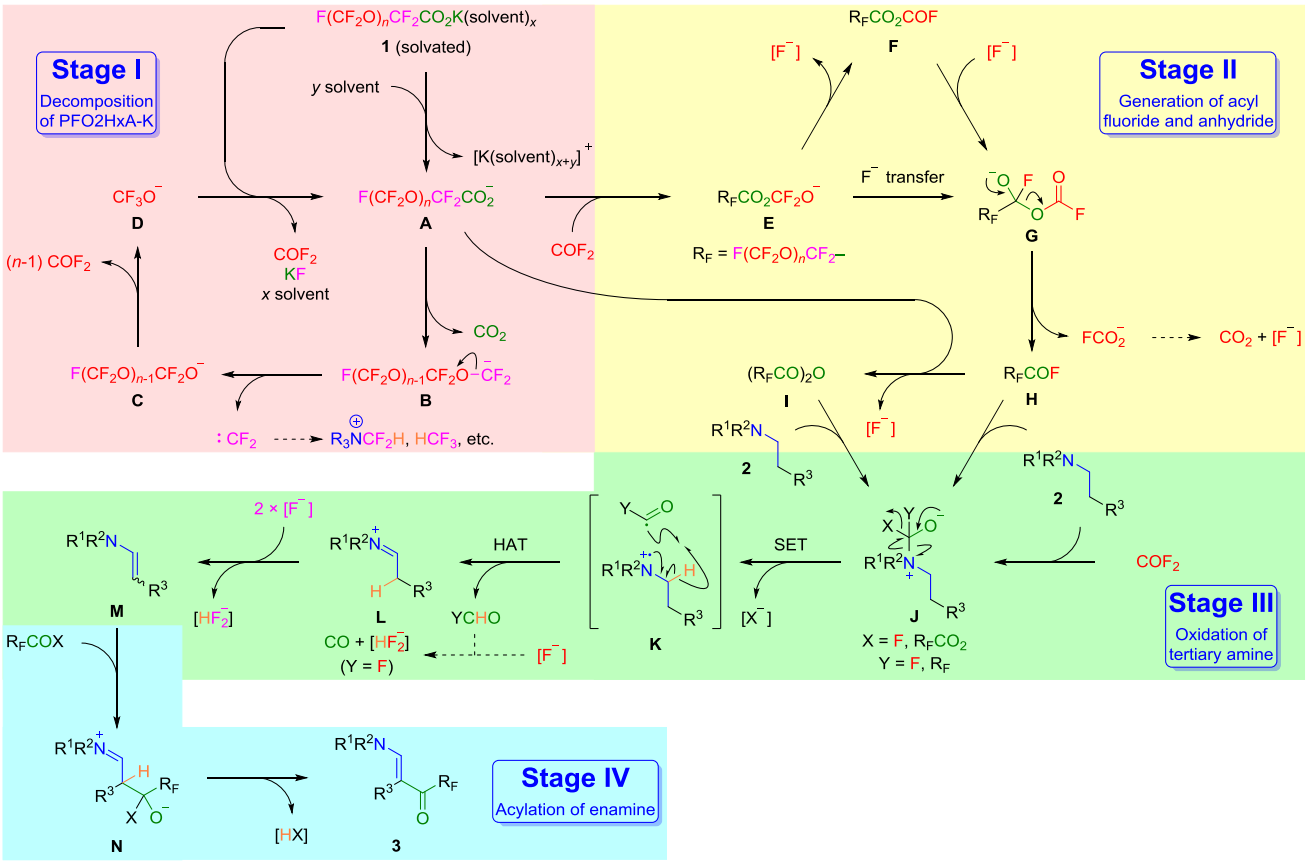


Figure 1 Proposed reaction mechanism.

fluoride **H**. Anhydride **I** may also be generated in the presence of excess **A**. Thereafter in stage III, the highly electron-poor acyl derivatives (COF_2, **H** and **I**) dehygrogenate **2** possibly *via* an SET and thence a hydrogen atom transfer (HAT) process, resulting in iminium **L**. With the aid of simultaneously produced potassium fluoride, **L** further deprotonates to provide enamine **M**, forming a nucleophilic site *β* to nitrogen. Acylation of **M** then proceeds readily with either **H** or **I** to afford the thermodynamic *trans*-enaminone product **3** (Figure 1, stage IV).

Conclusions

In summary, we have developed a facile synthetic approach to furnishing *trans*-2-(disubstituted-amino)alkenyl polyoxyperfluoroalkyl ketones from tertiary amines and PFECA salts featuring consecutive "–CF_2O–" units. The reaction is applicable to broad substrate scope, and a yield of up to 84% was observed. The reaction mechanism was proposed involving the heat-promoted *in situ* generation of COF_2, polyoxyperfluoroacyl fluorides and anhydrides which serve as key intermediates for the SET-based oxidation and acylation of amines.

It is worth mentioning that the novel perfluoroether-modified enaminone products are scarcely accessible by other methods, and may be applied as promising precursors of bioactive compounds and surfactants. Besides, as (hetero)difluoroacetates ($XCF_2CO_2^-$), PFECA salts may find their undeveloped use as a novel class of difluorocarbene precursors[26] and for the construction of –CF_2CO_2– segments[27] in the future work.

Experimental

Typical procedure for the synthesis of enaminone 3b. To an oven-dried 10 mL Schlenk tube equipped with a magnetic stir bar were charged tri-*n*-hexylamine (**2a**, 136 μL, 0.40 mmol, 1.0 equiv.), $F(CF_2O)_2CF_2CO_2K$ (**1b**, 227 mg, 0.80 mmol, 2.0 equiv.) and anhydrous acetonitrile (0.5 mL) under an argon atmosphere. The reaction was carried out upon vigorous stirring at 85 °C in an oil bath for 6 h. After the reaction was completed, the resulting mixture was cooled to room temperature and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (PE : EA = 50 : 1, *V*/*V*) to afford the pure product **3b** as a yellow oil (119.5 mg, 60%).

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.70055.

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