



Aza-tricycles containing a perfluoroalkyl group: synthesis, structure and fluorescence†

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Perfluoroalkyl-containing aza-tricycles have been prepared in one synthetic operation *via* an ambient light-promoted three-component reaction of β -oxo esters, perfluoroalkyl iodide and DBU. Intramolecular C–F...O and double C–H...F weak interactions and intermolecular C–H...O and C–H... π hydrogen bondings were observed partly due to the incorporation of the perfluoroalkyl group. The perfluoroalkylated non-planar aza-tricycles exhibit interesting room-temperature AIE fluorescence and acid-induced fluorescence enhancement characters.

Multicomponent reactions provide strategically challenging and synthetically useful methods for constructing unique carbo/heterocyclic frameworks from relatively simple molecules.¹ In the past few years, photo-induced multicomponent reactions have received more and more attention.^{1h} Recently, we reported an ambient light-promoted three-component reaction of active methylene compounds, perfluoroalkyl iodides and guanidines/amidines, which provides an efficient and practical entry to perfluoroalkylated pyrimidines.² In further research, we investigated the three-component reaction of β -oxo ester, perfluoroalkyl iodide and cyclic amidines like 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). As a result, perfluoroalkyl-containing fused aza-tricycles, *i.e.*, diazacyclohepta[*de*]naphthalen-4-ones were obtained under mild conditions (room temperature and ambient light).³ In this cascade reaction, DBU plays a dual role of both a base and a C,N-dinucleophile. DBU has been long known and utilized as a non-nucleophilic base,⁴ as well as a nucleophilic reagent (N-nucleophile,⁵

C-nucleophile,⁶ or C,N-dinucleophile⁷). The resulting perfluoroalkylated intramolecular donor-acceptor (D–A) type aza-tricycles exhibit interesting aggregation-induced emission (AIE) fluorescence properties⁸ and acid-induced fluorescence enhancement character.⁹ Herein, we would like to communicate results on the synthesis, structural elucidation and fluorescence properties of these aza-tricyclic compounds.¹⁰

The initial investigation was conducted on the condition optimization with the model reaction of ethyl benzoylacetate (**1a**), perfluorobutyl iodide (**2a**, 1.1 equiv.), and DBU (**3a**, 1.1 or 3.3 equiv.) (Table 1). The reaction in DMF proceeded quickly at room temperature, affording the diazacyclohepta[*de*]naphthalen-4-one **4a** in 24% yield (entry 1).¹¹ With 3.3 equiv. of DBU, the yield was increased to 53% (entry 2). An uncyclized by-product **5** was successfully isolated, which can be regarded as

Table 1 Optimization of the reaction conditions^a

Entry	Base (equiv)	Solvent	T (°C)	t (h)	Yield ^b (%)
1	DBU (1.1)	DMF	rt	0.5	24
2	DBU (3.3)	DMF	rt	0.5	53
3	DBU (3.3)	DMF	0 – rt	2	61
4	DBU (3.3)	MeCN	0 – rt	16	37 ^c
5	DBU (3.3)	DMSO	0 – rt	16	36
6	DBU (3.3)	DCM	0 – rt	16	35
7	DBU (3.3)	Toluene	0 – rt	16	30
8 ^d	DBU (3.3)	DMF/DCM	0 – rt	16	78
9 ^e	DBU (3.3)	DMF/DCM	0 – rt	16	83
10 ^f	DBU (3.3)	DMF/DCM	0 – rt	24	30

^a Reaction conditions: **1a** (0.1 mmol), **2a** (1.1 equiv.) and **3a** (1.1 or 3.3 equiv.) in solvent (0.5 mL) under ambient light. ^b Isolated yield. ^c Compound **5** was obtained as the main product. ^d DMF/DCM = 1/1 (volume ratio) was used in entries 8–10. ^e Under a N₂ atmosphere. ^f In the dark.

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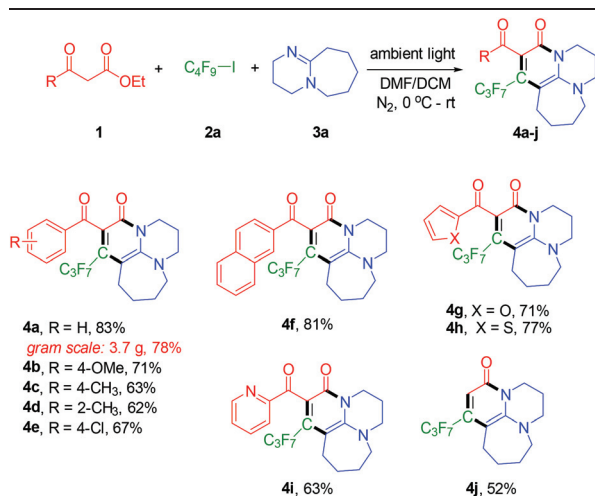
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the precursor of product **4a**. The reaction solution turned deep red immediately when conducting the reaction at room temperature, and a complex mixture was obtained within 30 min. Thus, the reaction was performed in an ice-water bath first, followed by warming the reaction solution to room temperature gradually. The yield of **4a** could be increased to 61% (entry 3). The solvent screening indicates that MeCN, DMSO, DCM and toluene were less efficient than DMF (entries 4–7). In the reaction system, uncyclized compound **5** was often observed in significant amounts, which is due to the poor solubility of **5** in common organic solvents. Thus, we tried to add DCM into DMF to minimize the content of precursor **5**. As a result, a mixture of DMF/DCM (1/1, volume ratio) may give **4a** in 78% isolated yield (entry 8). The reaction conducted under a N₂ atmosphere is cleaner and the yield of **4a** may reach up to 83% (entry 9). All the reactions were carried out under ambient light conditions. Comparatively, the reaction in the dark led to significantly decreased yields (entry 10), indicating that visible light plays a vital role in promoting the reaction.

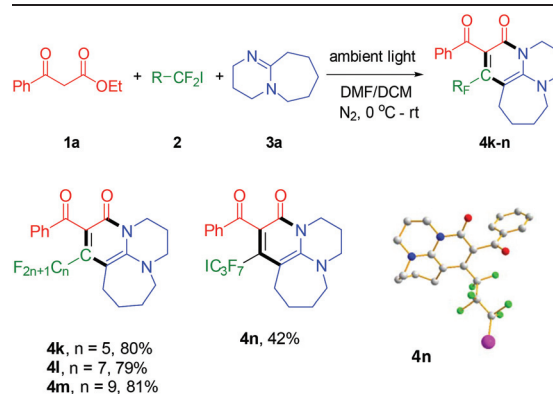
With the optimized conditions in hand (Table 1, entry 9), we set out to examine the reaction scope. A range of active methylene compounds were subjected to the reaction sequence (Table 2). α -Aroyl esters (R = Ph, 4-OMeC₆H₅, 4-MeC₆H₅, 2-MeC₆H₅, 4-ClC₆H₅ and 2-naphthyl) afforded the corresponding perfluoroalkylated aza-tricycles **4a–f** in moderate to high yields. Products **4g–i** containing a heteroaryl group (R = 2-furyl, 2-thienyl and 2-pyridyl) were also prepared in 63–77% yields. The reaction of β -keto ester containing an alkyl substituent like CF₃ with **2a** (1.1 equiv.) and DBU (3.3 equiv.) proceeded well, giving the corresponding 4-perfluoropropyl aza-tricycle **4j** in 52% yield, in which detrifluoroacetylation was observed.¹² To demonstrate the scalability of this protocol, gram-scale synthesis of **4a** was achieved (3.7 g, 78% yield, see Scheme S1† for details).

Table 2 Scope of active methylene compounds^{a,b}



^a Reaction conditions: **1** (0.1 mmol), **2a** (1.1 equiv.) and **3a** (3.3 equiv.) in DMF/DCM (1 : 1, volume ratio). ^b Isolated yields.

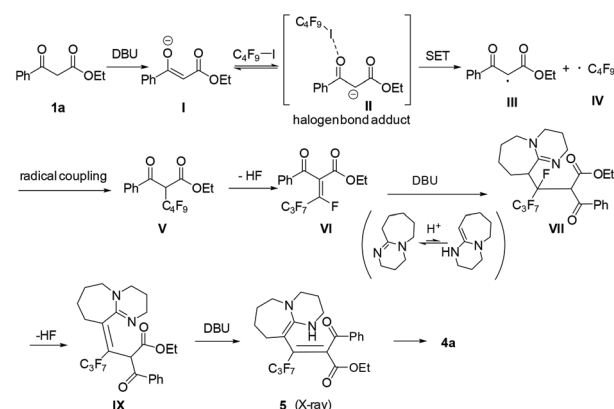
Table 3 Scope of perfluoroalkyl halides^{a,b}



^a Reaction conditions: **1a** (1.0 mmol), **2** (1.1 equiv.) and **3a** (1.1 equiv.) in MeCN (0.5 mL). ^b Isolated yields.

Next, we turn our attention to the scope of perfluoroalkyl halides. As shown in Table 3, a variety of perfluoroalkyl iodides with different chain lengths were suitable substrates in this multicomponent reaction, affording the corresponding perfluoroalkylated **4k–m** ($n = 5, 7, 9$) in good yields. Interestingly, 1,4-diiodoperfluorobutane was also a good partner for this reaction, giving product **4n** in 42% yield, with a pendent iodine atom at the end of the perfluoroalkyl chain.¹¹ The results described above demonstrated the substrate scope, functional group tolerance, and efficiency of the photo-promoted three-component reaction, which provided a new and efficient protocol for the construction of perfluoroalkyl tricyclic compound **4**.¹³

On the basis of the control experiments (see Scheme S2†), along with our previous result,² a tandem radical–polar mechanism for the three-component reaction is proposed (Scheme 1), which involves a sequence of SET (derived from the *in situ* formed halogen bond adduct, *i.e.*, EDA complex¹⁴), radical cross-coupling, HF elimination,¹⁵ Michael addition with DBU as a carbon nucleophile, and intramolecular aza-cyclization. In the ambient-light-promoted and halogen bond



Scheme 1 Possible mechanism for the formation of **4a**.

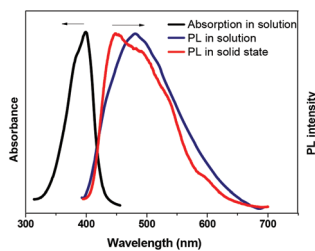


Fig. 1 Absorption and photoluminescence (PL) spectra of **4a** in DCM solution (concentration: 10^{-5} M) and in the solid state (excitation wavelength: 365 nm).

adduct-enabled three-component process, perfluoroalkylated aza-tricycles are assembled in formal $[2 + 1 + 3]$ annulation, with 2 C–C bond and 1 C–N bonds built up.

Interestingly, such types of aza-tricycles exhibit fluorescence properties. The optical properties of compound **4a** were examined. The absorption spectrum of **4a** in DCM solution reveals a maximum absorption peak at 395 nm, with a shoulder peak at 384 nm, which can be attributed to the intramolecular charge transfer (ICT) transition (Fig. 1). Upon photoexcitation at 365 nm, compound **4a** shows weak emission peaking at 498 nm in DCM solution. The Stokes shift between the absorption and emission spectra of **4a** was *approx.* 103 nm. The emission spectrum of **4a** in the powder state is broad and slightly blue-shifted, with the emission maximum at 448 nm and shoulder peaks at 491 and 594 nm, respectively. It was found that compound **4a** gives virtually faint fluorescence in dilute acetone solution. With increasing the concentration of the poor solvents such as water, the fluorescence intensity increases substantially and reaches a maximum peaking at 440 nm in the 70% water/acetone mixture (see Fig. 2). The fact of weak emission in solution but strong emission in the solid state indicates **4a** to have an aggregation-induced emission (AIE) character. Moreover, aza-tricycle **4a** is very sensitive to acid. An acid-induced fluorescence enhancement was observed upon gradual addition of HCl to **4a** in DCM (Fig. 3), which would find potential application as a fluorescent sensor for *in vivo* and *in vitro* analyses.¹⁶ The fluorescence enhancement may be reasoned by the protonation of the carbonyl group in the molecule, leading to remarkable intramolecular charge transfer.

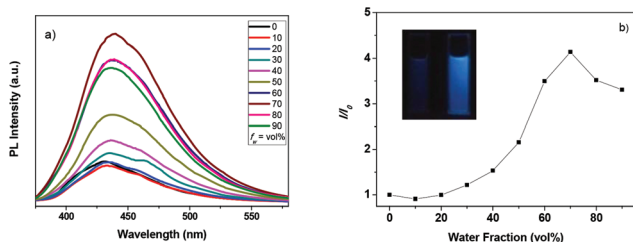


Fig. 2 (a) PL spectra of **4a** in acetone and acetone/water mixtures. (b) Plot of PL peak intensity vs. water fraction (f_w) of the aqueous mixture; inset: photographs of **4a** in acetone and its suspension in acetone/water mixtures with $f_w = 70\%$ under UV illumination.

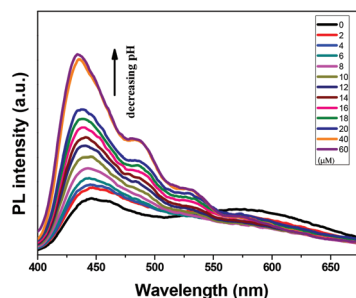


Fig. 3 PL spectra excited at 365 nm of **4a** in the presence of different concentrations of HCl in MeCN solution ($[4a] = 20 \mu\text{M}$, $[\text{HCl}] = 2.0, 4.0, 6.0, 8.0, 10.0, 12.0, 14.0, 16.0, 18.0, 20.0, 40.0,$ and $60.0 \mu\text{M}$).

The lifetime of compound **4a** was found to be around 2.11 ns in the powder state (Fig. S1†).¹⁷

To better understand the solid-state photophysical properties, we scrutinized the packing model of **4a** in the crystal-line state (Fig. 4). Fig. 4a and b show the molecular structure of uncyclized compound **5** (no emission in the solid state) and cyclized compound **4a**, respectively. The latter adopt a slightly twisted conformation, and the seven-membered aliphatic ring lies out of the plane of the conjugated molecular backbone. Intramolecular C–F \cdots O (2.89 Å) and double C–H \cdots F (2.37, 2.61 Å) weak interactions are observed. This indicates that cyclization leads to a rigid structure, compared to the flexible, unlocked counterpart **5**. Fig. 4c depicts the intermolecular packing of compound **4a**. The non-planar tricyclic structures are arranged in a loose manner, and no π – π intermolecular interactions were observed. Both C–H \cdots O (2.47 Å) and C–H \cdots π (2.86 Å) hydrogen bonds exist. Thus, an interesting cage-like architecture is formed comprising four **4a** molecules. In one word, the nature of the AIE character corresponding to non-planar perfluoroalkylated aza-tricyclic derivatives may arise both from the rigid molecular backbone and efficient inter-

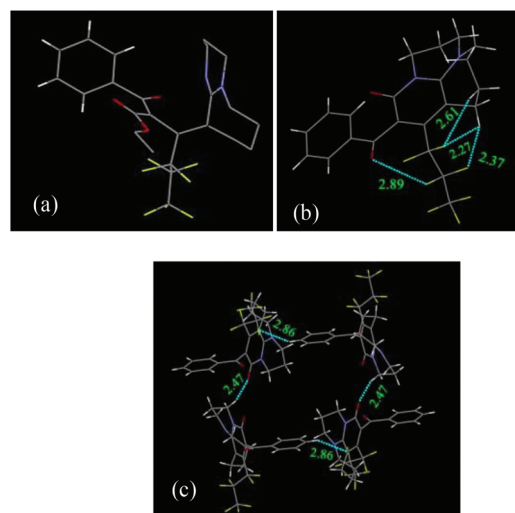


Fig. 4 Single crystal structures of **5** (a), **4a** (b) and molecular packing in crystals of **4a** (c).

molecular and intramolecular weak interactions. Rigidification *via* the chemical protocol and weak electrostatic interactions may lead to restricted rotation and motion within single molecule and molecular aggregates, thus inhibiting non-radiative decay and amplifying fluorescence emission.

Conclusions

In summary, we have synthesized new perfluoroalkyl-containing aza-tricycles that exhibit aggregation-induced emission and acid-induced fluorescence enhancement characters. The three-component reaction features high efficiency, very mild conditions and simple operation. The introduction of the perfluoroalkyl group enables intramolecular C–F \cdots O and double C–H \cdots F weak interactions and intermolecular C–H \cdots O and C–H \cdots π hydrogen bondings. The structure–AIE fluorescence property relationship was clarified and the rigidity of the molecular architecture as well as intramolecular and intermolecular interactions was responsible for the amplified AIE fluorescence in the D–A type non-planar aza-tricycle system.

Conflicts of interest

The authors declare no competing financial interest.

Acknowledgements

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