



Facile synthetic protocols for perfluoroalkyl-substituted diazapentaphenes



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ABSTRACT

Novel syntheses of 13,14-bis(perfluoroalkyl)-substituted 5,8-diazapentaphene derivatives were realized by such a facile two-step protocol as consecutive benzyne insertion into C(O)–NH bonds of *p*-phenylene-bis(perfluoroalkanamides), followed by Friedel–Crafts type cyclization reaction, yielding the corresponding title compounds especially for the case of Rf=CF₃ or C₂F₅. Additionally, an alternative approach based on condensation of cyclohexane-1,4-dione with (*o*-aminophenyl) perfluoroalkyl ketones, followed by dehydrogenation enabled us to effectively access to the same final products in better yields.

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1. Introduction

Nitrogen-containing aromatics have been recognized as one of the most important classes of compounds due to their contribution to remarkable developments in various fields, including pharmaceuticals and agrochemistry as well as electronic and optical technologies.¹ Among representative pentacyclic heteroaromatic compounds in the latter category, 5,8-diazapentaphene (dibenzo [*b,j*][4,7]phenanthroline) derivatives, containing nitrogen atoms at the 5 and 8-positions with a crescent shape are particularly of great importance due to their potential ability to stabilize synthetic DNA triple or quadruple helices by means of aromatic stacking interactions.² Moreover, such compounds with substituents at the 13 and 14 positions have been considered as a new class of helical substrates due to the strong distortion of the aromatic core caused by the steric repulsion between them, which can be promising entries as chiral ligands and optical materials.³ However, their synthetic studies have not been carried out adequately and, therefore, are highly desirable.⁴

Our recent attention has directed toward development of effective synthetic protocols of perfluoroalkyl (Rf)-substituted

polycyclic aromatic hydrocarbons since such moieties possibly affect an effective decrease of their HOMO and LUMO energy levels as well as systematic alignment by steady intermolecular electrostatic interactions between electrostatically-positive Rf-attached rings and relatively negative others. Very recently, we have successfully exploited an efficient synthetic protocol of Rf-possessing linear acenes and revealed that as our expectation, Rf moieties incorporated in the targets played an important role for molecular arrangement in the crystal phase.⁵ During the course of our study, we unexpectedly observed the formation of 13,14-bis(perfluoroalkyl)-5,8-diazapentaphene derivatives (Fig. 1), which to the best of our knowledge, has been unprecedented so far. In this paper are disclosed our detailed two independent synthetic routes to these compounds with two Rf groups at the 13 and 14

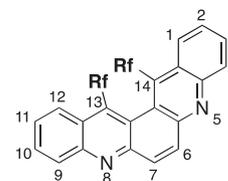


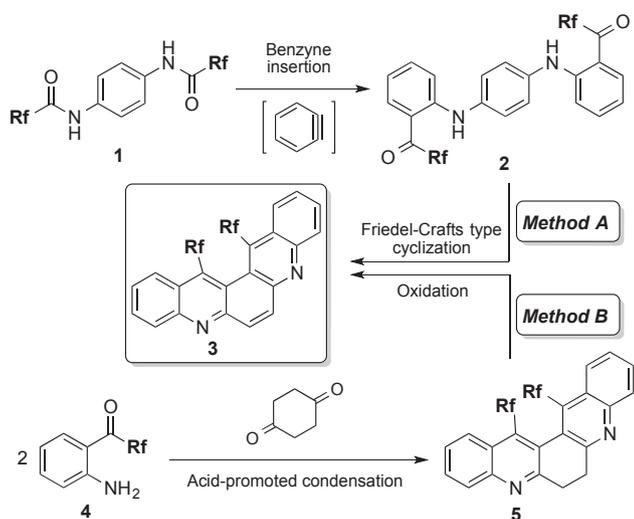
Fig. 1. 13,14-Bis(perfluoroalkyl)-5,8-diazapentaphene derivatives.

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positions. Moreover, their unique structural characterization in a solid state was also described.

2. Results and discussion

Our synthetic protocols for the target compounds, 13,14-bis(perfluoroalkyl)-5,8-diazapentaphenes **3**, were based on facile and simple two-step procedures (Scheme 1) either from *p*-phenylene-bis(perfluoroalkanamides) **1** or (*o*-aminophenyl) perfluoroalkyl ketones **4** as substrates: thus, benzyne insertion into the C(O)–NH bond in **1**, followed by Friedel–Crafts type cyclization (Method A), or acid-promoted condensation of cyclohexane-1,4-dione with **4**, followed by dehydrogenative oxidation (Method B).



Scheme 1. Synthetic plans for 13,14-bis(perfluoroalkyl)-5,8-diazapentaphene derivatives.

Initial examination for Method A was started as shown in Scheme 1, and the starting substrates, *p*-phenylene-bis(perfluoroalkanamides) **1**, were prepared in 56–89% yields from sulfuric acid salt of *p*-phenylenediamine and perfluoroalkanyl chloride or the corresponding anhydride.⁶ The subsequent benzyne insertion into the amide C–N bonds⁷ in **1a** (Rf: CF₃) was carried out according to the reported procedure. Thus, **1a** was subjected to a solution with a small excess amount (2.4 equiv) of 2-(trimethylsilyl)phenyl triflate (**6**) in the presence of 4.0 equiv of CsF in MeCN at room temperature for 4 h, while the desired reaction was unfortunately not occurred in our hand at all,⁸ resulting recovery of **1a** in a large amount.

Therefore, we attempted re-examination of this process using 2,2,2-trifluoroacetanilide (**7a**) as the model substrate. The results are summarized in Table 1. Thus, **7a** was treated with 1.2 equiv of **6** in the presence of 2.4 equiv of fluoride source in MeCN at room temperature for 4 h, and employment of CsF, TBAF, or KF led to unsatisfactory results (entries 1–3). On the contrary, combination of KF/18-crown-6 was found to be somewhat effective for the present reaction, giving the corresponding *o*-(phenylamino)phenyl trifluoromethyl ketone (**8a**)⁹ in 37% yield (entry 4). As shown in entries 4–8, THF was proved to be the solvent of choice among MeCN, DME, CH₂Cl₂ and toluene, leading to **8a** in 47% yield. After a couple of screenings on reaction temperature and time, as well as quantities of reagents, the best result (67% NMR yield) was eventually obtained when the benzyne insertion was conducted with 2.4 equiv of **6** in the presence of 4.8 equiv of KF and 18-crown-6 in THF at 50 °C for 12 h (entry 10).

Table 1
Optimization of reaction conditions for benzyne insertion

Entry	Fluoride source (equiv)	Solvent	Yield of 8a (%) ^a	Recovery of 7a (%) ^a
1 ^b	CsF (2.4)	MeCN	0	82
2	TBAF (2.4)	MeCN	16	70
3	KF (2.4)	MeCN	0	88
4	KF/18-c-6 ^c (2.4)	MeCN	37	51
5	KF/18-c-6 (2.4)	THF	47	50
6	KF/18-c-6 (2.4)	DME	40	43
7	KF/18-c-6 (2.4)	CH ₂ Cl ₂	20	57
8	KF/18-c-6 (2.4)	Toluene	5	95
9 ^d	KF/18-c-6 (2.4)	THF	50	38
10 ^{d,e}	KF/18-c-6 (4.8)	THF	67	0

^a Yield and recovery were determined by ¹⁹F NMR.

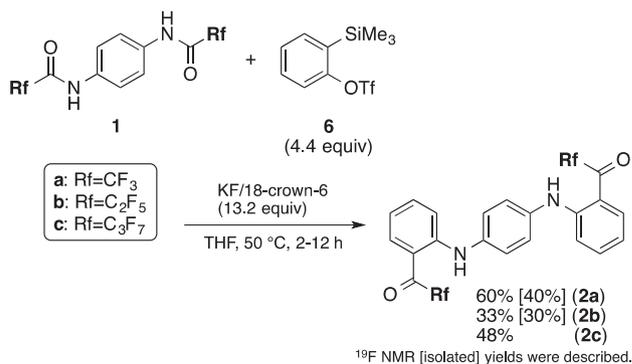
^b Performed under the conditions reported in Ref. 7b.

^c 18-Crown-6.

^d Carried out at 50 °C for 12 h.

^e With 2.4 equiv of **7**.

On the basis of the optimized reaction conditions thus determined, benzyne insertion using *p*-phenylene-bis(perfluoroalkanamides) **1** was performed with slight modifications, which was illustrated in Scheme 2.



Scheme 2. Benzyne insertion into *p*-phenylene-bis(perfluoroalkanamides) **1**.

On treating **1a** with 4.4 equiv of **6** in the presence of 13.2 equiv each of KF and 18-crown-6 in THF at 50 °C for 12 h, the double benzyne insertion took place smoothly to furnish the corresponding **2a** in 60% NMR yield (40% isolated yield). Similarly, pentafluoroethyl- (**2b**) or heptafluoropropyl derivatives (**2c**) were also successfully obtained in moderate yields.

At the next stage, our interest was attracted to the product selectivity between crescent (**3a**) and linear forms (**10a**) at the Friedel–Crafts cyclization step of **2a** (Scheme 3). As a possible route, the intermediary **9a** after first cyclization of **2a** would be further converted to the linear-form **10a** via cation intermediate **Int-B** by C–C bond construction at the β-position of the acridine ring. On the other hand, the crescent form **3a** might be yielded by cyclization at the α-carbon via **Int-A**. On actual performance of the Friedel–Crafts reaction in a trifluoroacetic acid (CF₃CO₂H) at reflux temperature for 5 h, the exclusive formation of the crescent form **3a** was observed in 48% isolated yield.

Subsequently, our attention was focused on modification of the above synthetic process by elimination of the purification process

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