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A facile carbene route to 2-fluoro-2-pyrrolines via fluorinated azomethine ylides

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Abstract

2-Fluoro-2-pyrrolines have been prepared by a domino reaction of difluorocarbene with *N*-substituted ketimines in the presence of fumaronitrile, malenitrile or dimethyl maleate, involving azomethine ylide formation, 1,3-dipolar cycloaddition, and dehydrofluorination. The reactions of *1H-dibenzo[b,e]*azepine and 3,4-dihydroisoquinolines with difluorocarbene in the presence of fumaronitrile proceed with the formation of fluorinated 1H-dibe*n*zo[*c,f*]pyrrolo[1,2-*a*]azepine and pyrrolo[2,1-*a*]isoquinoline derivatives. The yields of 2-fluoro-2-pyrrolines depend mostly on their resistance to chromatographic work-up and are higher for 5,5-disubstituted pyrrolines compared to 5-monosubstituted derivatives.

Keywords: Pyrroles; Carbenes; Ylides; Cycloaddition; Domino reaction

1. Introduction

Pyrrole and its derivatives are a class of compounds among the most important heterocycles in synthetic and pharmacological practice [1]. In recent years, special attention has been paid to fluorine-containing pyrroles as potentially biologically active compounds. A number of synthetic approaches to fluoropyrroles have been proposed, such as direct fluorination of pyrrole derivatives [2,3], refunctionalisation by Schiemann reaction [4], heterocyclisation of fluorinated precursors [5], and 1,3-dipolar cycloadditions involving either fluorinated azomethine ylides [6–8] or fluorinated dipolarophiles [9,10]. A more challenging problem in this field is synthesis of partly hydrogenated pyrroles with fluorine attached to the ring-carbon atom, e.g. 2-fluoro-2-pyrrolines. These compounds may offer interest not only in terms of biological activity, but also, having a fairly reactive fluorine atom, as synthetic building blocks. However, no convenient synthetic procedures for these compounds have been reported. Two types of transformations are known, resulting in isolation of 2-pyrrolines with a fluorine atom in the position 2 of the ring [11,12]. The photolytic ring contraction of *N-substituted* perfluoroazepines to form *N-substituted* perfluoro-3a,5a-dihydrocyclobuta[*b*]pyrroles cannot be considered an acceptable synthetic route to 2-fluoro-2-pyrrolines, since this is a particular reaction characteristic of perfluorinated cyclobuta[*b*]pyrroles [11]. The reaction of *N*-methylpyrrolidone with carbonyl fluoride in the presence of cesium fluoride provides 2-fluoro-1-methyl-2-pyrroline-3-carbonyl fluoride in a yield as low as 4% [12].

2. Results and discussion

In this communication we report a convenient synthesis of 2-fluoro-2-pyrrolines by a domino reaction of difluorocarbene with imines in the presence of but-2-enedioic acid derivatives. As starting imines we used acyclic Schiff bases **1a**,**b** [13], **1c** [14] as well as compounds **6** [15], **10** [16] containing an endocyclic C=N bond. Difluorocarbene was generated *in situ* by reduction of CF_2Br_2 with lead powder in the presence of tetrabutylammonium bromide (TBAB). The reaction of imines **1a–c** with difluorocarbene in the presence of fumaronitrile, malenitrile, or dimethyl maleate resulted in isolation, after chromatographic purification, of 2-fluoro-2-pyrrolines **4a–c**, **5** (Scheme 1). The mechanism of the reaction depicted in Scheme 1 involves attack of difluorocarbene onto the nitrogen lone pair of the imine to give azomethine ylide **2** followed by 1,3-dipolar cycloaddition of the latter to the olefin and spontaneous dehydrofluorination of intermediate difluoropyrrolidine **3**. All the synthesized

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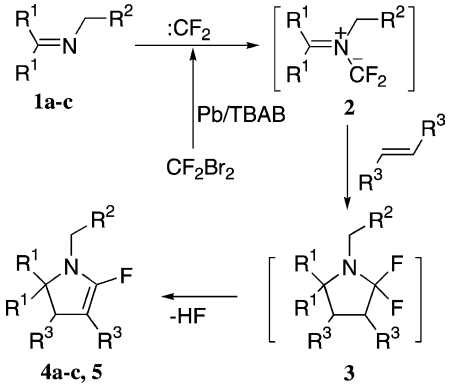


Scheme 1.

compounds, except for pyrroline **5**, are quite stable toward chromatographic purification and storage at 5 °C. To isolate compound **5**, both the reaction mixture before chromatography and the eluants were treated with Et_3N. The isolated product was stored in a refrigerator at −18 °C. Moreover, the yield of pyrroline **5** was improved by using active lead [7] instead of lead powder due to much reduced reaction time (Table 1).

The reaction of cyclic analogue of ketimines **1a–c**, 1-phenyl-3,4-dihydroisoquinoline **6a**, with difluorocarbene in the presence of fumaronitrile proceeded in a similar way but gave a mixture of stereoisomers **7a**, **8a** in a total yield of 59%. The stereochemical assignment for adducts **7a** and **8a** were based on NOE experiments. The *cis* relative configuration of 1-CN and 10b-Ph in **7a** and its *trans* relationship in **8a** were clearly demonstrated by enhancement of the signal of aromatic proton at H-10 (14%) in **7a** and the absence of NOE in **8a** when the resonance corresponding to the protons at H-1 of both compounds was irradiated. This assignment is also confirmed by an 11% NOE enhancement between H-1 and *ortho*-protons of benzene ring in isomer **8a** and the absence of this correlation in isomer **7a** (Scheme 2, Table 2).

Fluoropyrrolines derived from aldimines and its cyclic analogues, e.g. compounds **6b**, are generally less stable than those derived from ketimines. Nevertheless, they can also be successfully synthesized and isolated provided one prevents formation of a trace amount of acid during work-up. Thus, in the reaction of compound **6b** with difluorocarbene in the presence of fumaronitrile a stereoisomeric mixture of fluoropyrrolines **7b**, **8b** could be isolated in a total yield 39% by use of Et_3N-containing eluent for column chromatographic separation. Stereochemical assignment of diastereomeres **7b**, **8b** rests on the magnitude of the J (H^1, H^{10b}) values in the ^1H NMR spectra: 9.9 Hz in isomer **8b** is characteristic of *cis* configuration and 4 Hz in isomer **8b** for *trans* configuration [17].

Cyclic imine **10** containing an aryl substituent at the nitrogen atom gave, under the same conditions, fluoropyrrolines **11** and **12**. Compound **11** that has a larger J (H^1, H^{13b}) coupling constant (10.6 Hz) in the ^1H NMR spectrum was assigned *cis* configuration of the C^1–C^{13b}, and isomer **12**, *trans* configuration [J (H^1, H^{13b}) 7.9 Hz], which is nicely consistent with the magnitudes of the $\angle HC^1C^{13b}H$ dihedral

Table 1
Preparation of pyrrolines **4a–c**, **5**

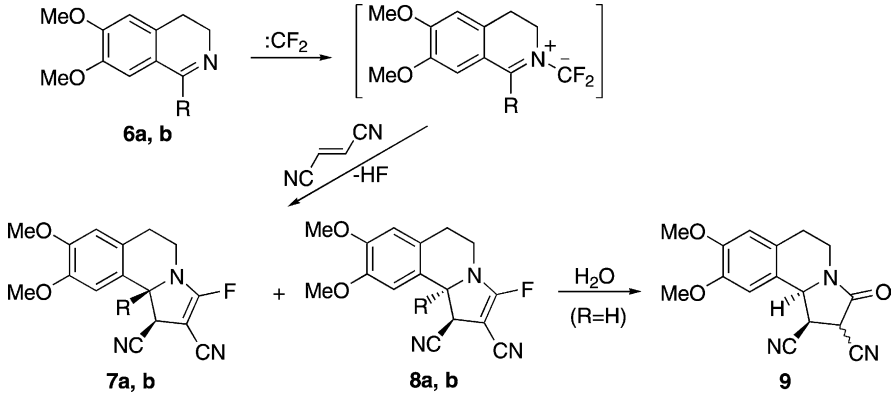
Imine	R^1	R^2	R^3	Dipolarophile	Reaction time (h)	Yield (%)
1a	Ph	H	CN	Fumaronitrile	7	84 (**4a**)
1a	Ph	H	CN	Malenitrile	14	74 (**4a**)
1b	Ph	CH_2Ph	CN	Fumaronitrile	17	64 (**4b**)
1c	Ph	CO_2Me	CN	Fumaronitrile	18	63 (**4c**)
1a	Ph	H	CO_2Me	Dimethyl maleate	3[a]	64 (**5**)

[a] Reaction with active lead.

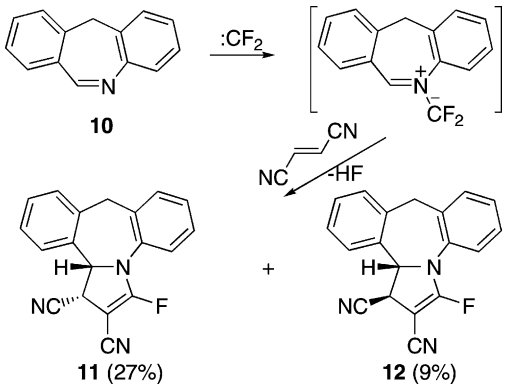
Table 2
Preparation of pyrrolines **7a**,**b**, **8a**,**b**

Imine **6**	R	Reaction time (h)	Yield of **7** (%)	Yield of **8** (%)
a	Ph	25	31	28
b	H	36	26	–[a]

[a] Pyrroline (**8b**) was not isolated as a pure sample because of its hydrolysis to 3-oxo-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile **9** obtained in 9% yield.



Scheme 2.



Scheme 3.

angles, calculated at the PM3 level (24° and 109°, respectively) (Scheme 3).

In conclusion, a facile approach to 2-fluoro-2-pyrrolines has been suggested that relies on a carbene-derived azomethine ylide formation/1,3-dipolar cycloaddition domino sequence. The yields of 2-fluoro-2-pyrrolines depend mostly on their resistance to chromatographic work-up and are higher for those obtained from ketimines compared to aldimine-derived products.

3. Experimental

3.1. General

Melting points were determined on a hot stage microscope (Boetius) and are uncorrected. IR spectra were recorded on a Carl-Zeiss UR 20 spectrometer. ^{1}H NMR spectra were recorded on a Bruker DPX 300 spectrometer at 300 MHz with internal standard TMS ($\delta = 0$) and ^{13}C NMR spectra at 75 MHz with internal standard $CDCl_3$ ($\delta = 76.7$). Elemental analysis was performed on a Hewlett-Packard 185B CHN-analyser. Mass spectra were obtained using a MX-1303 instrument. Methylene chloride was dried by distillation over phosphorus pentoxide. Silica gel Merck 60 was used for column chromatography. Sodium borohydride, lead acetate, dibromodifluoromethane, tetrabutylammonium bromide, fumaronitrile and dimethyl maleate were obtained commercially.

The reagent ratios used were the same as in the typical procedure, unless otherwise specified.

3.2. 5-Fluoro-1-methyl-2,2-diphenyl-2,3-dihydropyrrole-3,4-dicarbonitrile (**4a**) (typical procedure)

A flask containing freshly prepared lead powder (1.7 g, 8.2 mmol) and methylene chloride (15 cm^3) was charged with Bu_4NBr (2.7 g, 8.4 mmol), *N*-benzhydrylidene-*N*-methylamine **1a** (0.51 g, 2.6 mmol), fumaronitrile (0.41 g, 5.2 mmol) and CBr_2F_2 (1.72 g, 8.3 mmol). The flask was tightly stoppered, immersed in a sonic cleaner and irradiated with ultrasound at 40–45 °C until the lead was consumed completely (reaction time given in Table 1). The solvent was removed under reduced pressure, and the residue was separated by chromatography on silica gel to afford after recrystallisation 0.66 g (84%) of pyrroline **4a** as a colourless solid: mp 143–145 °C (Et_2O–CH_2Cl_2). Anal. Calcd. for $C_{19}H_{14}FN_3$: C, 75.23; H, 4.65; N 13.85. Found: C, 75.84; H, 4.79; N, 13.75. IR ($CHCl_3$); ν 2220 (C≡N), 1660 cm^{-1} (C=C). ^{1}H NMR ($CDCl_3$): δ 2.60 (3H, s, CH_3), 4.77 (1H, d, $^4J_{HF} = 3.5$ Hz, H-3), 7.27–7.37 (10H, *m*, H_{arom}). ^{13}C NMR ($CDCl_3$): δ 28.3 (d, $^3J_{CF} = 2.8$ Hz, CH_3), 44.6 (d, $^3J_{CF} = 4.4$ Hz, C-3), 53.3 (d, $^2J_{CF} = 13.8$ Hz, C-4), 75.7 (C-2), 112.9 (d, $^3J_{CF} = 3.9$ Hz, CN), 115.3 (d, $^4J_{CF} = 2.2$ Hz, CN), 126.8, 127.7, 128.7, 128.9, 129.3, 129.3, 136.3, 138.4 (C_{arom}), 165.2 (d, $^1J_{CF} = 286.4$ Hz, C-5).

The analogous reaction of imine **1a** (0.51 g, 2.6 mmol) with maleonitrile (0.41 g, 5.2 mmol) gave 0.58 g (74%) of pyrroline **4a**.

3.3. 5-Fluoro-1-phenethyl-2,2-diphenyl-2,3-dihydropyrrole-3,4-dicarbonitrile (**4b**)

Prepared by the typical procedure from *N*-benzhydrylidene-*N*-phenethylamine **1b** (0.7 g, 2.45 mmol) and fumaronitrile (0.38 g, 4.9 mmol). Yield 0.62 g (64%). Colourless solid, mp 194–195 °C (Et_2O–CH_2Cl_2). Anal. Calcd. for $C_{26}H_{20}FN_3$: C, 79.37; H, 5.12; N 10.58. Found: C, 79.32; H, 5.12; N, 10.68. IR ($CHCl_3$); ν 2215 (C≡N), 1660 cm^{-1} (C=C). ^{1}H NMR ($CDCl_3$): δ 1.75–1.81, 2.32–2.38, 3.01–3.16, 3.36–3.46 (4H, *m*, $2CH_2$), 4.86 (1H, d, $^4J_{HF} = 2.6$ Hz, H-3), 6.83–7.60 (15H, *m*, H_{arom}). ^{13}C NMR ($CDCl_3$): δ 34.3 (d, $^4J_{CF} = 0.6$ Hz, CH_2), 44.9 (d, $^3J_{CF} = 4.4$ Hz, C-3), 46.0 (NCH_2), 52.6 (d, $^2J_{CF} = 14.4$ Hz, C-4), 75.9 (C-2), 112.9 (d, $^3J_{CF} = 3.8$ Hz, CN), 115.1 (CN), 126.6, 126.9, 127.8, 128.1, 128.4, 128.7, 129.1, 129.4, 129.7, 136.6, 136.8, 139.7 (C_{arom}), 165.1 (d, $^1J_{CF} = 286.9$ Hz, C-5).

3.4. Methyl (3,4-dicyano-5-fluoro-2,2-diphenyl-2,3-dihydropyrrol-1-yl)acetate (**4c**)

Prepared by the typical procedure from methyl *N*-benzhydrylideneglycinate **1c** (1.04 g, 4.1 mmol) and fumaronitrile (0.64 g, 8.2 mmol). Yield 0.93 g (63%). Colourless solid, mp 178–180 °C (Et_2O). Anal. Calcd. for $C_{21}H_{16}FN_3O_2$: C, 69.80; H, 4.46; N 11.63. Found: C, 69.85; H, 4.60; N, 11.64. IR ($CHCl_3$); ν 2220 (C≡N), 1755 (C=O), 1655 cm^{-1} (C=C). ^{1}H NMR ($CDCl_3$): δ 3.38 (3H, s, CH_3), 3.75 and 3.98 (2H, *AB-q*, $J = 18.3$ Hz, CH_2), 4.86 (1H, d, $^4J_{HF} = 3.5$ Hz, H-3), 7.31−7.37 (10H, *m*, H_{arom}). ^{13}C NMR ($CDCl_3$): δ 44.0 (CH_2), 44.4 (d, $^3J_{CF} = 4.4$ Hz, C-3), 52.1 (CH_3), 54.3 (d, $^2J_{CF} = 12.7$ Hz, C-4), 75.8 (C-2), 112.4 (d, $^3J_{CF} = 3.9$ Hz, CN), 115.0 (d, $^4J_{CF} = 2.8$ Hz, CN), 127.2, 127.7, 128.8, 129.4, 129.5, 136.6, 138.2 (C_{arom}), 164.8 (d, $^1J_{CF} = 289.1$ Hz, C-5), 166.4 (C=O).

3.5. Dimethyl 5-fluoro-1-methyl-2,2-diphenyl-2,3-dihydropyrrole-3,4-dicarboxylate (**5**)

Prepared by the typical procedure from *N*-benzhydrylidene-*N*-methylamine **1a** (0.64 g, 3.3 mmol) and dimethylmaleate (0.95 g, 6.6 mmol) using active lead [7] instead of lead powder. Chromatographic separation was accomplished by use of hexane-ethyl acetate mixture as eluent doped with 0.01% of Et_3N. Yield 0.77 g (64%). Colourless solid, mp 128–130 °C (Et_2O–hexane). Anal. Calcd. for $C_{21}H_{20}FNO_4$: C, 68.28; H, 5.46; N 3.79. Found: C, 68.30; H, 5.50; N, 3.76. IR ($CHCl_3$); *v* 1760, 1705 (C=O), 1650 cm^{-1} (C=C) ^1H NMR ($CDCl_3$): δ 2.52 (3H, s, NCH_3), 3.07 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 4.71 (1H, d, $^4J_{HF} = 3.5$ Hz, H-3), 7.22−7.40 (10H, *m*, H_{arom}). ^{13}C NMR ($CDCl_3$): δ 28.1 (d, $^3J_{CF} = 3.3$ Hz, NCH_3), 50.4 (OCH_3), 51.1 (OCH_3), 57.1 (d, $^3J_{CF} = 3.9$ Hz, C-3), 74.3 (C-2), 76.9 (d, $^2J_{CF} = 7.2$ Hz, C-4), 127.4, 127.6, 127.7, 128.1, 128.5, 136.8, 140.4 (C_{arom}), 162.8 (d, $^1J_{CF} = 288$ Hz, C-5), 163.7 (d, $J_{CF} = 5$ Hz, C=O), 170.8 (d, $J_{CF} = 2.8$ Hz, C=O).

3.6. 3-Fluoro-8,9-dimethoxy-10b-phenyl-1,5,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,2-dicarbonitriles (**7a**) and (**8a**)

Prepared by the typical procedure from 6,7-dimethoxy-1-phenyl-3,4-dihydroisoquinoline **6a** (0.8 g, 3.0 mmol) and fumaronitrile (0.94 g, 12.0 mmol) (reaction time 25 h). (1*RS*,10b*SR*)-isomer **7a**. Yield 0.35 g (31%). Light-yellow prisms, mp 196–198 °C (EtOAc). Anal. Calcd. for $C_{22}H_{18}FN_3O_2$: C, 70.39; H, 4.83; N 11.19. Found: C, 70.41; H, 4.93; N, 11.17. IR ($CHCl_3$); *v* 2217 (C≡N), 1665 cm^{-1} (C=C). ^1H NMR ($CDCl_3$): δ 2.53–2.61, 2.91–3.03, 3.14–3.23, 3.70–3.78 (4H, *m*, $2CH_2$), 3.90 (3H, s, CH_3), 3.97 (3H, s, CH_3), 4.73 (1H, d, $^4J_{HF} = 2.5$ Hz, H-1), 6.65 (1H, s, H-10), 6.83 (1H, s, H-7), 7.40 (5H, s, H_{Ph}). ^{13}C NMR ($CDCl_3$): δ 26.4 (C-6), 37.9 (C-5), 44.1 (d, $^3J_{CF} = 5.5$ Hz, C-1), 52.6 (d, $^2J_{CF} = 13.8$ Hz, C-2), 55.7 (CH_3), 56.1 (CH_3), 70.2 (C-10b), 108.9, 111.6 (C-7, C-10), 113.0 (d, $^3J_{CF} = 4.4$ Hz, CN), 115.7 (d, $^4J_{CF} = 2.8$ Hz, CN), 125.6, 127.1, 127.4, 128.4, 129.1, 137.5 (C-6a, C-10a, C_{Ph}), 147.8, 149.0 (C-9, C-10), 165.3 (d, $^1J_{CF} = 286.2$ Hz, C-3). (1*RS*,10b*RS*)-isomer **8a** was isolated in 28% yield (0.31 g) with 35% impurity of isomer (**7a**). ^1H NMR ($CDCl_3$): δ 2.71–2.77, 2.91–3.23, 3.70–3.81, (4H, *m*, $2CH_2$), 3.82 (3H, s, CH_3), 3.93 (3H, s, CH_3), 4.77 (1H, d, $^4J_{HF} = 4.4$ Hz, H-1),), 6.54 (1H, s, H-10), 6.70 (1H, s, H-7), 7.28–7.41 (5H, *m*, H_{Ph}). ^{13}C NMR ($CDCl_3$): δ 28.0 (C-6), 37.6 (C-5), 44.4 (C-1), 53.2 (d, $^2J_{CF} = 14.4$ Hz, C-2),), 55.5 (CH_3), 55.9 (CH_3), 68.6 (C-10b), 111.1, 111.4 (C-7, C-10), 113.2 (d, $^3J_{CF} = 4.4$ Hz, CN), 115.8 (d, $^4J_{CF} = 2.8$ Hz, CN), 124.2, 125.6, 125.9, 128.8, 129.1, 142.0 (C_{arom}), 147.6, 149.1 (C-9, C-10), 163.1 (d, $^1J_{CF} = 285.3$ Hz, C-3).

3.7. 3-Fluoro-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,2-dicarbonitriles (**7b**) and (**8b**)

Prepared by the typical procedure from 6,7-dimethoxy-3,4-dihydroisoquinoline **6b** (0.53 g, 2.8 mmol) and fumaronitrile (0.44 g, 5.6 mmol) (reaction time 47 h). (1*RS*,10b*RS*)-isomer **7b**. Yield 0.22 g (26%). Colourless solid, mp 191–193 °C (EtOAc). Anal. Calcd. for $C_{16}H_{14}FN_3O_2$: C, 64.21; H, 4.71; N 14.04. Found: C, 64.22; H, 4.65; N, 14.02. IR ($CHCl_3$); *v* 2220 (C≡N), 1650 cm^{-1} (C=C). ^1H NMR ($CDCl_3$): δ 2.61–2.68, 2.90–3.00, 3.22–3.31, 3.89–3.95 (4H, *m*, $2CH_2$), 3.89 (3H, s, CH_3), 3.92 (3H, s, CH_3), 4.03 (1H, dd, $J = 4.0$ Hz, $^4J_{HF} = 2.5$ Hz, H-1), 5.25 (1H, d, $J = 4.0$ Hz, H-10b), 6.59 and 6.61 (1H, s, H-7, H-10). ^{13}C NMR ($CDCl_3$): δ 26.7 (C-6), 37.3 (d, $^4J_{CF} = 5.3$ Hz, C-5), 40.4 (d, $^3J_{CF} = 1.1$ Hz, C-1), 55.1 (d, $^2J_{CF} = 14.8$ Hz, C-2), 55.6 (CH_3), 55.9 (CH_3), 61.4 (C-10b), 106.8, 111.3 (C-7, C-10), 112.5 (d, $J_{CF} = 5.0$ Hz, CN), 117.9 (d, $J_{CF} = 3.3$ Hz, CN), 123.8, 125.1, 148.7, 148.8 (C_{arom}), 166.0 (d, $^1J_{CF} = 285.8$ Hz, C-3). (1*RS*,10b*SR*)-isomer **8b**. ^1H NMR ($CDCl_3$): δ 2.71-3.91 (4H, *m*, $2CH_2$), 3.90 (6H, s, $2CH_3$), 4.33 (1H, dd, $J = 9.9$ Hz, $^4J_{HF} = 3.4$ Hz, H-1), 5.26 (1H, d, $J = 9.9$ Hz, H-10b), 6.21 and 6.31 (1H, s, H-7, H-10). Compound **8b** was detected in a mixture with **7b** by ^1H NMR spectroscopy after chromatographic work-up of the reaction mixture. Attempted separation from **7b** resulted in hydrolysis of **8b** to (1*RS*,10b*SR*)-8,9-dimethoxy-3-oxo-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile **9**. Compound **9**: yield 0.075 g (9%). Colourless solid, mp 205–208 °C ($CHCl_3$) (decomp.). Anal. Calcd. for $C_{16}H_{15}N_3O_3$: C, 64.64; H, 5.09; N 14.13. Found: C, 64.46; H, 5.18; N, 14.02. IR ($CHCl_3$); *v* 2260 (C≡N), 1740 (C=O). ^1H NMR ($CDCl_3$): δ 2.71–2.79, 2.89–3.00, 3.06–3.16, 4.38–4.44 (4H, *m*, $2CH_2$), 3.30 (1H, dd, $J = 11.9$ Hz, $J = 9.3$ Hz, H-1), 3.91 (3H, s, CH_3), 3.93 (3H, s, CH_3), 4.05 (1H, $J = 11.9$ Hz, C-2), 5.02 (1H, d, $J = 9.3$ Hz, H-10b), 6.67 and 7.00 (1H, s, H-7, H-10). ^{13}C NMR ($CDCl_3$): δ 27.4 (C-6), 36.3, 38.1, 38.2 (C-1, C-2, C-5), 55.7, 55.8 (CH_3), 57.0 (C-10b), 106.3, 111.7 (C-7, C-10), 113.3, 116.1 (CN), 122.6, 125.0, 148.6, 149.1 (C_{arom}), 160.4 (C-3). EIMS 70 eV, *m/z* (rel. int.): 297 $[M]^+$ (58), 191 $[M\text{-}CH(CN)CH(CN)CO]^+$ (100), 176 $[191\text{-}CH_3]^+$ (25).

3.8. 3-Fluoro-9,13b-dihydro-1H-dibenzo[c,f]pyrrolo-[1,2-a]azepine-1,2-dicarbonitriles (**11**) and (**12**)

Prepared by the typical procedure from *11H-dibenzo-[b,e]*azepine **10** (0.5 g, 2.6 mmol) and fumaronitrile (0.4 g, 5.2 mmol) (reaction time 86 h). (1*RS*,10b*SR*)-Isomer **11**. Yield 0.21 g (27%). Colourless solid, mp 154–156 °C (EtOAc–CH_2Cl_2). Anal. Calcd. for $C_{19}H_{12}FN_3$: C, 75.74; H, 4.01; N, 13.95. Found: C, 75.63; H, 4.04; N, 14.01. IR ($CHCl_3$); *v* 2220 (C≡N), 1650 cm^{-1} (C=C). ^1H NMR ($CDCl_3$): δ 3.65 (1H, d, $J_{HH} = 14.6$ Hz, H-9), 4.18 (1H, dd, $^4J_{CF} = 3.5$ Hz, $J_{HH} = 10.6$ Hz, H-1), 4.56 (1H, d,

J_{HH} = 14.6 Hz, H-9), 5.48 (1H, d, J_{HH} = 10.6 Hz, H-13b), 7.28–7.38 (8H, *m*, H_{arom}). ^{13}C NMR ($CDCl_3$): δ 37.7 (d, $^3J_{CF}$ = 4.6 Hz, C-1), 38.4 (C-9), 55.1 (d, $^2J_{CF}$ = 12.6 Hz, C-2), 66.8 (C-13b), 112.3 (d, $^3J_{CF}$ = 3.4 Hz, CN), 117.2 (d, $^3J_{CF}$ = 2.3 Hz, CN), 125.4, 127.0, 127.9, 128.0, 128.7, 128.8, 129.0, 130.4, 133.2, 133.3, 135.3, 138.7 (C_{arom}), 163.5 (d, $^1J_{CF}$ = 287.4 Hz, C-3). (1*RS*,10b*RS*)-isomer **12**. Yield 0.07 g (9%). Colourless solid, mp 258–260 °C (Et_2O–CH_2Cl_2). Anal. Calcd. for $C_{19}H_{12}FN_3$: C, 75.74; H, 4.01; N, 13.95; Found: C, 75.98; H, 4.08; N, 14.01. IR ($CHCl_3$); *v* 2220 (C≡N), 1650 cm^{-1} (C=C). ^1H NMR: δ 3.61 (1H, d, J_{HH} = 13.7 Hz, H-9), 4.30 (1H, dd, $^4J_{CF}$ = 2.9 Hz, J_{HH} = 7.9 Hz, H-1), 4.82 (1H, d, J_{HH} = 13.7 Hz, 9-H), 5.40 (1H, d, J_{HH} = 7.9 Hz, H-13b), 7.02–7.40 (8H, *m*, H_{arom}). ^{13}C NMR (DMSO-d_6): δ 37.3 (d, $^3J_{CF}$ = 3.5 Hz, C-1), 37.9 (C-9), 55.3 (d, $^2J_{CF}$ = 12.6 Hz, C-2), 68.7 (C-13b), 114.9 (d, $^3J_{CF}$ = 3.4 Hz, CN), 117.9 (CN), 126.7, 128.3, 128.8, 129.4, 129.6, 129.7, 131.1, 132.3, 134.1, 137.7, 140.1 (C_{arom}), 163.5 (d, $^1J_{CF}$ = 287.4 Hz, C-3).

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