

Polyhalogenated heterocyclic compounds Part 46. Multifunctional heterocycles from bromofluoropyridine derivatives[☆]

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Dedicated to Prof. Karl Christe on the occasion of his 65th birthday

Abstract

2,4,6-Tribromo-3,5-difluoro-pyridine **1** was used as the starting material for the synthesis of a variety of multifunctional pyridine derivatives. For example, nucleophilic substitution reactions involving appropriate difunctional nucleophiles gave products resulting from intramolecular cyclisation processes and the organolithium derivative **9**, readily prepared from **1**, could be trapped by various of electrophilic reagents. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

Polysubstituted pyridine derivatives are notoriously difficult to synthesise and the problem grows with the number and different substitution patterns of the substituents [2]. Nevertheless, relatively little attention has been focused on the use of polyhalogenated pyridine derivatives as appropriate starting compounds for the synthesis of multifunctional derivatives and this paper demonstrates the relevance of some of the chemistry of 2,4,6-tribromo-3,5-difluoropyridine **1** in this context.

There is a considerable chemistry derived from nucleophilic substitution in pentafluoro- and pentachloro-pyridine that has already been described [3–6], but comparatively little that is directed to the synthesis of multifunctional compounds. However, recently we reported that **1** could be used for this purpose and highlighted the different preferences for reaction of **1** with various hard and soft nucleophiles which led to attack at sites attached to fluorine and

bromine, respectively [7]. In preliminary experiments, we also demonstrated that sites attached to bromine can be activated in palladium catalysed processes [7].

2. Results and discussion

Reaction of sodium phenoxide with **1** led exclusively to attack at carbon attached to the 3- and 5-fluorine substituents to give products **2** and **3** (Scheme 1) depending on the proportion of phenoxide used (one and two equivalents, respectively). However, when resorcinol was used the disubstituted derivative **4**, arising from reaction of resorcinol and two equivalents of the pyridine derivative **1**, was isolated as the major product. It is clear, however, that the remaining sites attached to fluorine also compete for resorcinol, because a significant amount of intractable material was formed which we assume to be polyaryl ethers.

Using catechol, the situation is more interesting because cyclic systems **5** and **6** are produced (Scheme 2). It is reasonable to assume that **5** and **6** are formed by first reaction at the 3-position, displacing fluoride ion, but then intramolecular displacement of bromine occurs and this process obviously competes favourably with intermolecular displacement of fluorine from another molecule of **1**. However,

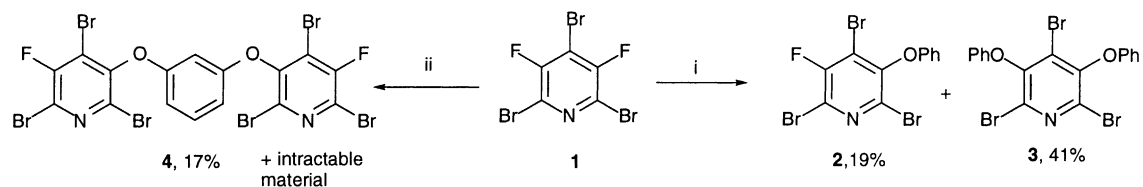
[☆]For part 45, see [1].

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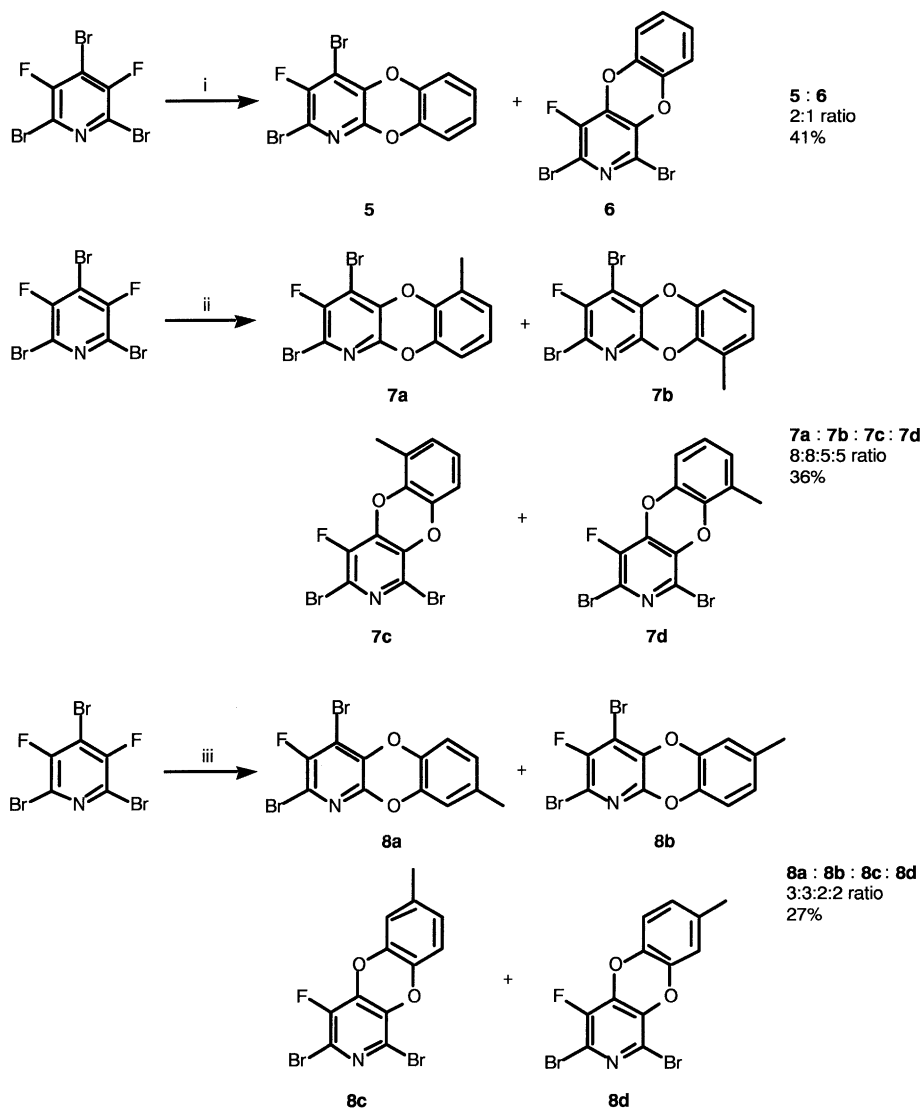
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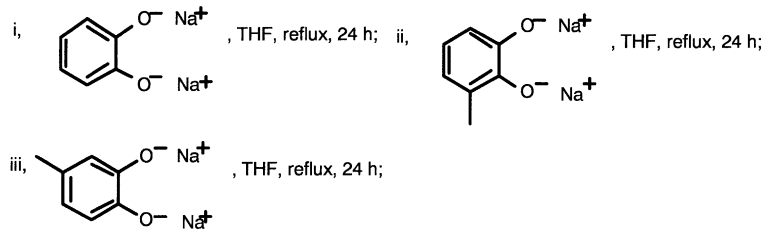
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Scheme 1. Reagents and conditions: (i) PhONa (two equivalents), THF, reflux, 24 h; (ii) 1,3-NaO-C₆H₄-ONa, THF, reflux, 24 h.



Scheme 2
Reagents and Conditions



Scheme 2. Reagents and conditions: (i) *n*-BuLi, Et₂O, -78 °C; (ii) H₂O, -78 °C to room temperature; (iii) Me₃SiCl, -78 °C to room temperature; (iv) CO₂ gas, -78 °C to room temperature; (v) PhCOCl, -78 °C to room temperature; (vi) CH₃C₆H₄COCl, -78 °C to room temperature.

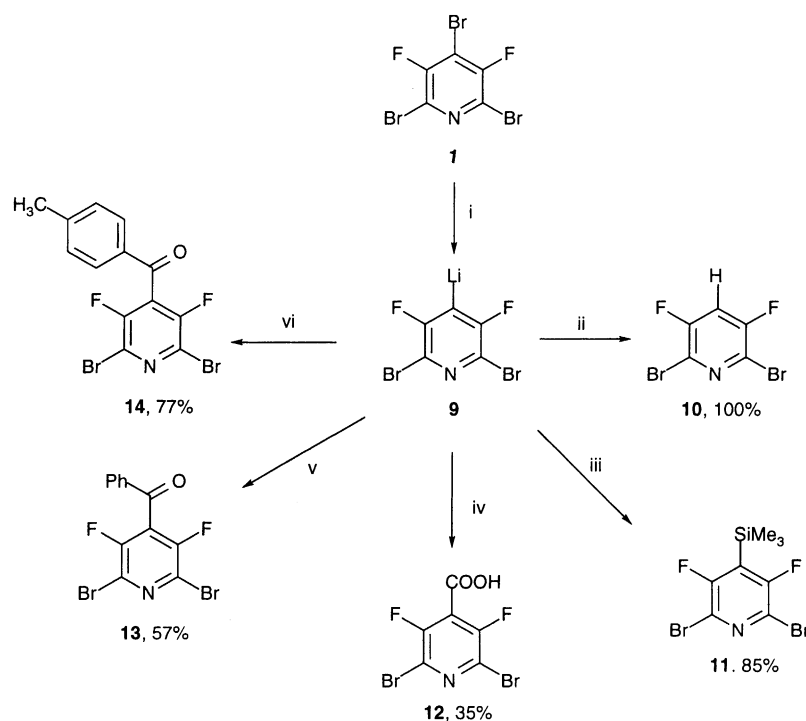
some intractable material is formed which is attributed to polymer formation. It could be argued that a 2:1 ratio for intramolecular displacement of bromine at the 2- versus 4-positions, giving **5** and **6**, respectively, reflects a less crowded site at the 2-position, because the directing effect of nitrogen would normally slightly favour attack at the 4-position. A similar effect is observed in reactions of 3-methyl catechol and 4-methyl catechol with **1**; each gave mixtures of products **7a–d** and **8a–d**, respectively, where, again, the cyclisation step appears to slightly favour attack at the 2-position.

Reaction of **1** with *n*-butyllithium in diethylether at $-78\text{ }^{\circ}\text{C}$ gives rapid bromine–lithium exchange and the lithio derivative **9** is sufficiently stable at low temperature to react with a variety of electrophiles (Scheme 3). Reaction of **9**

with water gave **10**, which demonstrated that bromine–lithium exchange proceeds quantitatively while silylation and carboxylation, giving **11** and **12**, respectively, may also be achieved.

Surprisingly, however, reactions of lithio derivative **9** with acroyl chlorides stopped at the ketone stage and **13** and **14** were isolated as crystalline solids, suitable for X-ray structural analysis. The most reasonable explanation of this unusual result is that approach of nucleophiles to the carbonyl group in both **13** and **14** is sterically impeded by the attached aryl groups and this is supported by the crystal structure of **14** (Fig. 1).

More convincing, however, is the fact that reaction of **9** with acetyl chloride does indeed proceed beyond the ketone



Scheme 3. Reagents and conditions: (i) *n*-BuLi, Et₂O, $-78\text{ }^{\circ}\text{C}$; (ii) CH₃COCl, room temperature.

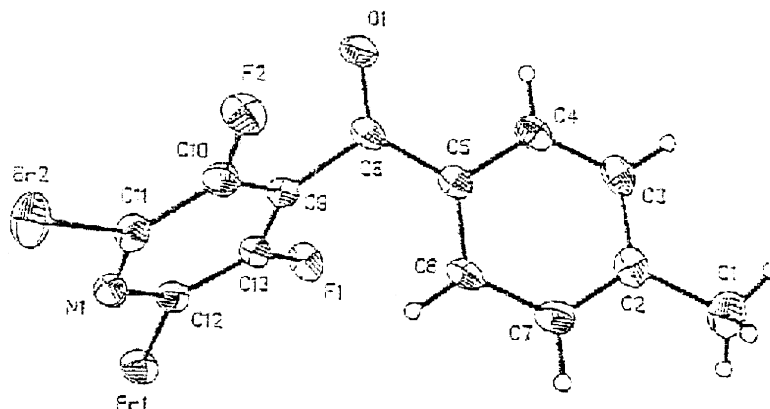
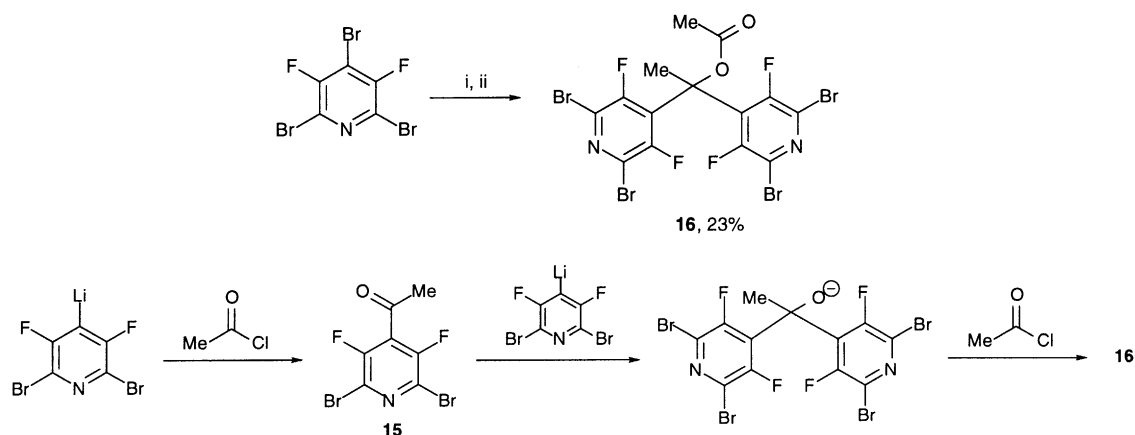


Fig. 1. X-ray crystal structure of 2,6-dibromo-3,5-difluoro(4-pyridyl) methylphenyl ketone **14**.

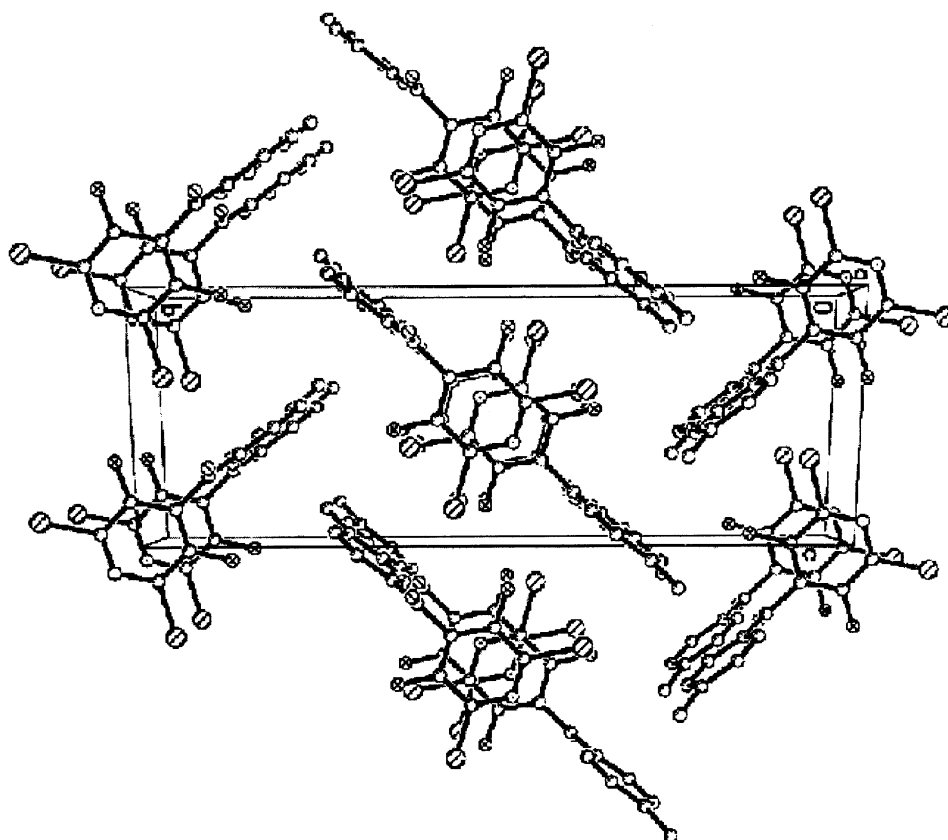


Scheme 4.

15 stage giving the acyl ester **16** of the corresponding alcohol by a mechanism outlined in Scheme 4. Obviously, in this case, **15** is much less sterically hindered to further nucleophilic attack. A similar process involving a lithiated perfluoroheterocyclic system was reported by Coe and Rees during the course of this work [8].

In summary, **9** may be trapped by a range of electrophiles leading to various products depending on the electrophilic system, thus extending the synthetic utility of perbromo-fluoro heterocycles such as **1**.

A single crystal of **14** was grown that was suitable for X-ray crystallography. We expected to observe significant face-to-face π - π interaction between the electron poor pyridine ring and the relatively electron rich aryl ring, as is observed in many systems involving a combination of highly fluorinated aromatic derivatives and hydrocarbon aromatic systems [9]. However, as shown in Figs. 1 and 2, the molecules in the crystal form stacks along the *a*-direction that are arranged in a 'herring bone' configuration in which the pyridine subunits adopt an edge-to-face configuration

Fig. 2. Crystal stacking arrangement of 2,6-dibromo-3,5-difluoro(4-pyridyl) methylphenyl ketone **14**.

with the aromatic ring of the adjacent molecule. Furthermore, at first sight, it appears that face-to-face π - π interactions between adjacent pyridine rings is occurring but the calculated interplanar distance (3.68 Å) is too large for any such interaction to be significant. Consequently, the crystal structure observed is probably due to the adoption of the most favourable stacking arrangement and the minimisation of unfavourable electron pair interactions.

3. Experimental

All solvents were dried before use by literature procedures. NMR spectra were recorded on a Varian VXR 400S NMR spectrometer with tetramethylsilane and trichlorofluoromethane as internal standards and deuteriochloroform as solvent, unless otherwise stated. In ^{19}F NMR spectra, upfield shifts are quoted as negative. Coupling constants are given in Hz. Mass spectra were recorded a Fisons VG Trio 1000 spectrometer coupled with a Hewlett-Packard 5890 series II gas chromatograph. IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrometer using KBr plates while elemental analyses were obtained on either a Perkin-Elmer 240 or a Carlo Erba elemental analyser. Melting points were recorded at atmospheric pressure and are uncorrected. Column chromatography was performed on silica gel (Merck No. 1-09385) and TLC analysis was performed on silica gel TLC plates (Merck). 2,4,6-Tribromo-3,5-difluoro-pyridine was synthesised according to the literature procedure [7].

3.1. Reactions with oxygen nucleophiles

3.1.1. General procedure

Sodium metal was added to a solution of the alcohol or diol in THF (50 ml) and the mixture was heated at reflux temperature until complete dissolution of the sodium. 2,4,6-Tribromo-3,5-difluoro-pyridine was added and the reaction mixture heated at reflux temperature for a further 24 h. On cooling, THF was removed by distillation and the residue added to water. Extraction into dichloromethane, drying (MgSO_4) and evaporation of the solvent gave a solid which was purified by column chromatography on silica gel.

3.1.2. Reaction with phenol (two equivalents)

Sodium (0.28 g, 12 mmol), phenol (0.95 g, 10 mmol) and 2,4,6-tribromo-3,5-difluoro-pyridine (1.5 g, 4.3 mmol) in THF (50 ml) gave a white solid (2.26 g) which, after purification by column chromatography on silica gel using dichloromethane/hexane (1:4) as eluant, gave 2,4,6-tribromo-3,5-diphenoxy-pyridine **3** (0.87 g, 41%) as a white crystalline solid; mp 172.2–173.9 °C; (found: C, 41.7; H, 2.1; N, 2.8. $\text{C}_{17}\text{H}_{10}\text{Br}_3\text{NO}_2$ requires: C, 40.8; H, 2.0; N, 2.8%); δ_{H} 6.7–7.3 (m, ArH); δ_{C} 115.4 (s, Ar_{ortho}), 123.7 (s, Ar_{para}), 127.2 (s, C-4), 130.2 (s, Ar_{meta}), 132.6

(s, C-2), 148.0 (s, C-3), 155.8 (s, Ar_{ipso}); m/z (EI^+) 503 (M^+ , 2%), 501 (M^+ , 7), 499 (M^+ , 7), 498 (M^+ , 7), 497 (M^+ , 2), 77 (100).

3.1.3. Reaction with resorcinol

Sodium (0.07 g, 3 mmol), resorcinol (0.16 g, 10 mmol) and 2,4,6-tribromo-3,5-difluoro-pyridine (1.5 g, 4.3 mmol) in THF (50 ml) gave a white solid (1.9 g) which, after purification by column chromatography on silica gel using dichloromethane/hexane (1:1) as eluant, gave 2,4,6-tribromo-3-fluoro-5-[3-(2,4,6-tribromo-5-fluoro(3-pyridyloxy))phenoxy]pyridine **4** (0.55 g, 17%) as a white crystalline solid; mp 239.5–245.3 °C; (found: C, 26.0; H, 0.7; N, 3.4. $\text{C}_{15}\text{H}_4\text{Br}_6\text{F}_2\text{N}_2\text{O}_2$ requires: C, 24.8; H, 0.5; N, 3.6%); δ_{H} 6.44 (2H, m, H-4,6), 7.16 (2H, m, H-2,5); δ_{C} 104.4 (s, Ar-2), 110.0 (s, Ar-4), 118.0 (d, $^2J_{\text{CF}}$ 21.3, C-4), 124.4 (d, $^2J_{\text{CF}}$ 25.9, C-2), 130.6 (s, C-6), 130.9 (s, Ar-5), 147.3 (s, C-5), 154.2 (d, $^1J_{\text{CF}}$ 262, C-3), 156.7 (s, Ar-1); δ_{F} -104.0 (s); m/z (EI^+) 780 (M^+ , 3%), 778 (M^+ , 17), 776 (M^+ , 44), 774 (M^+ , 60), 772 (M^+ , 45), 770 (M^+ , 18), 768 (M^+ , 3); and intractable material.

3.1.4. Reaction with catechol

Sodium (0.22 g, 9.5 mmol), catechol (0.47 g, 4.3 mmol) and 2,4,6-tribromo-3,5-difluoro-pyridine (1.5 g, 4.3 mmol) in THF (50 ml) gave a white solid (2.05 g) which, after purification by column chromatography on silica gel using dichloromethane/hexane (1:1) as eluant, gave a mixture consisting of 2,4-dibromo-3-fluorobenzo[e]pyridino[3,2-b]-1,4-dioxin **5** and 1,3-dibromo-4-fluorobenzo[e]pyridino[4,3-b]1,4-dioxane **6** (0.63 g, 41%) in the ratio 2:1 (measured by ^{19}F NMR integration of the crude reaction mixture) as a white crystalline solid; (found: C, 36.6; H, 1.1; N, 3.7. $\text{C}_{11}\text{H}_4\text{Br}_2\text{FNO}_2$ requires: C, 36.6; H, 1.1; N, 3.9%); δ_{H} 6.96 (m, ArH); δ_{F} -111.2 (s, **5**), -133.5 (s, **6**); m/z (EI^+) 363 (M^+ , 39%), 361 (M^+ , 75%), 359 (M^+ , 39), 50 (100); and intractable material.

3.1.5. Reaction with 3-methylcatechol

Sodium (0.11 g, 5 mmol), 3-methylcatechol (0.29 g, 2.3 mmol) and 2,4,6-tribromo-3,5-difluoro-pyridine (0.75 g, 4.3 mmol) in THF (50 ml) gave a white solid (0.93 g) which, after purification by column chromatography on silica gel using dichloromethane/hexane (1:1) as eluant, gave a mixture consisting of 2,4-dibromo-3-fluoro-6-methyl-benzo[e]pyridino[3,2-b]1,4-dioxin **7a**, 2,4-dibromo-3-fluoro-9-methyl-benzo[e]pyridino[3,2-b]1,4-dioxin **7b**, 1,3-dibromo-4-fluoro-6-methyl-benzo[e]pyridino[4,3-b]1,4-dioxane **7c** and 1,3-dibromo-4-fluoro-9-methyl-benzo[e]pyridino[4,3-b]1,4-dioxane **7d** (0.29 g, 36%) in a ratio 8:8:5:5 (measured by ^{19}F NMR integration of the crude reaction mixture) as a white crystalline solid; (found: C, 38.3; H, 1.5; N, 3.6. $\text{C}_{12}\text{H}_6\text{Br}_2\text{FNO}_2$ requires: C, 38.6; H, 1.6; N, 3.7%); δ_{H} 2.27, 2.28, 2.29 and 2.30 (3H, all s, CH_3), 6.8–7.0 (5H, m, Ar-H); δ_{F} -111.43 and -111.78 (both s, **7a** and **7b**), -133.66 and -133.69 (both s, **7c** and **7d**); m/z (EI^+) 377

(M^+ , 49%), 375 (M^+ , 100%), 373 (M^+ , 53%); and intractable material.

3.1.6. Reaction with 4-methylcatechol

Sodium (0.12 g, 5 mmol), 4-methylcatechol (0.29 g, 2.3 mmol) and 2,4,6-tribromo-3,5-difluoro-pyridine (0.75 g, 4.3 mmol) in THF (50 ml) gave a white solid (0.84 g) which, after purification by column chromatography on silica gel using dichloromethane/hexane (1:1) as eluant, gave a mixture consisting of 2,4-dibromo-3-fluoro-7-methyl-benzo[e]pyridino[3,2-b]1,4-dioxin **8a**, 2,4-dibromo-3-fluoro-8-methyl-benzo[e]pyridino[3,2-b]1,4-dioxin **8b**, 1,3-dibromo-4-fluoro-7-methyl-benzo[e]pyridino[4.3-b]1,4-dioxane **8c** and 1,3-dibromo-4-fluoro-8-methyl-benzo[e]pyridino[4.3-b]1,4-dioxane **8d** (0.22 g, 27%) in a ratio 3:3:2:2 (measured by ^{19}F NMR integration of the crude reaction mixture) as a white crystalline solid; (found: C, 38.6; H, 1.7; N, 3.7. $\text{C}_{12}\text{H}_6\text{Br}_2\text{FNO}_2$ requires: C, 38.6; H, 1.6; N, 3.7%); δ_{H} 2.27–2.3 (3H, overlapping s, CH_3); δ_{F} –111.45 and –111.59 (both s, **8a** and **8b**), –133.60 and –133.65 (both s, **8c** and **8d**); m/z (EI^+) 377 (M^+ , 27%), 375 (M^+ , 60%), 373 (M^+ , 28%), 39 (100); and intractable material.

3.2. Generation and reactions of 4-lithio-2,6-dibromo-3,5-difluoro-pyridine **9**

3.2.1. General procedure

A three necked flask, equipped with a low temperature thermometer, a drying tube and flushed with dry nitrogen, was charged with **1** and diethyl ether. The mixture was cooled to -78°C before *n*-butyllithium (1.6 M solution in hexanes) was added. The resulting solution, which gradually turned yellow in colour, was stirred at -78°C for 90 min. ^{19}F NMR analysis of the crude mixture indicated complete conversion of the starting material to 4-lithio-2,6-dibromo-3,5-difluoro-pyridine **9**; δ_{F} –89.7 (s). The electrophile was added to the cool solution and the mixture was allowed to warm to room temperature overnight. Addition of water, followed by extraction by dichloromethane (3×20 ml), drying (MgSO_4) and evaporation gave the crude product. Purification of the functional pyridine derivative was accomplished by column chromatography on silica gel, recrystallisation or vacuum sublimation, as indicated.

3.2.2. 2,6-Dibromo-3,5-difluoro-pyridine **10**

2,4,6-Tribromo-3,5-difluoro-pyridine (1.0 g, 2.84 mmol), *n*-butyllithium (1.9 ml, 3.55 mmol), diethyl ether (15 ml) and water (10 ml) gave, after sublimation, 2,6-dibromo-3,5-difluoro-pyridine **10** (0.55 g, 71%) as a white solid; mp 110 – 111°C ; (found: C, 22.2; N, 5.0; H, 0.4; Br, 58.3; F, 13.7. $\text{C}_5\text{HBr}_2\text{F}_2\text{N}$ requires: C, 22.2; N, 5.1; H, 0.3; Br, 58.6; F, 13.9%); δ_{C} 113.7 (t, $^2J_{\text{CF}}$ 23.9, C-4), 122.6 (X part of ABX, C-2), 155.4 (dd, $^1J_{\text{CF}}$ 270.5, $^3J_{\text{CF}}$ 4.9, C-3); δ_{H} 7.31 (t, 3JHF 6.3); δ_{F} –109.53 (d, 3JFH 7.1); m/z (EI^+) 271 (M^+ , 56%), 273 (M^+ , 100), 275 (56), 274 (5%).

3.2.3. 2-2,6-Dibromo-3,5-difluoro-4-trimethylsilyl-pyridine **11**

2,4,6-Tribromo-3,5-difluoro-pyridine (1.0 g, 2.84 mmol), *n*-butyllithium (1.9 ml, 3.55 mmol), diethyl ether (15 ml) and chlorotrimethylsilane (0.38 g, 3.5 mmol) gave, after column chromatography on silica gel using diethyl acetate/hexane (1:1) as eluant, 2-2,6-dibromo-3,5-difluoro-4-trimethylsilyl-pyridine **11** (0.82 g, 85%); mp 86 – 88°C ; (found: C, 27.8; H, 2.6; N, 3.4. $\text{C}_8\text{H}_9\text{Br}_2\text{F}_2\text{NSi}$ requires: C, 27.8; H, 2.60; N, 4.05%); δ_{C} 0.66 (s, CH_3), 122.4 (X part of ABX system, C-2), 127.4 (t, $^2J_{\text{CF}}$ 33.6, C-4), 158.5 (dd, $^1J_{\text{CF}}$ 257, $^3J_{\text{CF}}$ 8.4, C-3); δ_{H} 0.36 (s); δ_{F} –99.7 (s); m/z (EI^+) 347 (M^+ , 24), 345 (M^+ , 47), 343 (25), 77 (100%).

3.2.4. 2,6-Dibromo-3,5-difluoro-pyridine-4-carboxylic acid **12**

2,4,6-Tribromo-3,5-difluoro-pyridine (0.4 g, 1.14 mmol), diethyl ether (15 ml), *n*-butyllithium (0.76 ml, 1.42 mmol) and carbon dioxide gas (passed through the solution for 2 h) gave after the aqueous layer was acidified and extracted with ether, 2,6-dibromo-3,5-difluoro-pyridine-4-carboxylic acid **12** (0.12 g, 35%) as white crystals; mp 154 – 156°C ; (found: C, 22.8; N, 4.1; H, 0.3. $\text{C}_6\text{HBr}_2\text{F}_2\text{NO}_2$ requires: C, 22.7; N, 4.4; H, 0.3%); δ_{C} 106.4 (t, $^2J_{\text{CF}}$ 24.2, C-4), 123.4 (X part of ABX system, C-2), 152.6 (dd, $^1J_{\text{CF}}$ 270.4, $^3J_{\text{CF}}$ 3.9, C-3), 159.1 (s, COOH); δ_{H} 6.26 (bs, COOH); δ_{F} –110.56 (s); m/z (EI^+) 316 (M^+ , 100), 272 (M^+ –COOH, 100%).

3.2.5. 2,6-Dibromo-3,5-difluoro(4-pyridyl) phenyl ketone **13**

2,4,6-Tribromo-3,5-difluoro-pyridine (1.0 g, 2.84 mmol), *n*-butyllithium (1.9 ml, 3.55 mmol), diethyl ether (15 ml) and benzoyl chloride (0.61 g, 4.32 mmol) gave, after purification by column chromatography using dichloromethane/hexane (1:4) as eluant and recrystallisation from hexane, 2,6-dibromo-3,5-difluoro(4-pyridyl) phenyl ketone **13** (0.61 g, 57%) as a white solid; (found: C, 38.2; N, 3.6; H, 1.4. $\text{C}_{12}\text{H}_5\text{Br}_2\text{F}_2\text{NO}$ requires: C, 38.2; N, 3.7; H, 1.3%); δ_{C} 123.3 (X part of an ABX system, C-2), 126.24 (m, C-4), 129.5 (s, C-ortho), 130.3 (s, C-meta), 134.9 (s, C-ipso), 135.9 (s, C-para), 152.1 (dd, $^1J_{\text{CF}}$ 266.3, $^3J_{\text{CF}}$ 3.9, C-3), 184.5 (s, C=O); δ_{H} 7.5–7.7 (m, Ar–H); δ_{F} –112.24 (s); m/z (EI^+) 375 (M^+ , 7%), 377 (M^+ , 14), 379 (M^+ , 7).

3.2.6. 2,6-Dibromo-3,5-difluoro(4-pyridyl) 4-methylphenyl ketone **14**

2,4,6-Tribromo-3,5-difluoro-pyridine (1.0 g, 2.84 mmol), *n*-butyllithium (1.9 ml, 3.55 mmol), diethyl ether (15 ml) and *p*-toluoyl chloride (0.66 g, 4.26 mmol) gave, after recrystallisation, 2,6-dibromo-3,5-difluoro(4-pyridyl) 4-methylphenyl ketone **14** (0.85 g, 77%); mp 145 – 146°C ; (found: C, 39.9; H, 1.8; N, 3.6. $\text{C}_{13}\text{H}_7\text{Br}_2\text{F}_2\text{NO}$ requires: C, 39.9; H, 1.7; H, 4.0%); δ_{C} 26.9 (s, CH_3), 123.3 (X part of an ABX system, C-2), 126.5 (t, $^2J_{\text{CF}}$ 21.4, C-4), 130.1 (s, C-ortho), 130.3 (s, C-meta), 132.3 (s, C–Cz.dbnd6;O), 147.2 (s, C– CH_3), 152.0 (dd, $^1J_{\text{CF}}$ 258, $^3J_{\text{CF}}$ 1.9, C-3), 184

(s, C=O); δ_{H} 1.36 (3H, s, CH₃), 7.28 and 7.60 (4H, AB, J_{AB} 8.4, Ar–H); δ_{F} –112.28 (s); m/z (EI⁺) 389 (M^+ , 4%), 391 (M^+ , 8), 393 (4), 119 (100), 91 (55), 65.(52).

3.2.7. 1,1-Bis(2,6-dibromo-3,5-difluoro-4-pyridyl)ethyl acetate **16**

2,4,6-Tribromo-3,5-difluoro-pyridine (1.0 g, 2.84 mmol), *n*-butyllithium (1.9 ml, 3.55 mmol), diethyl ether (15 ml) and acetyl chloride (0.33 g, 4.26 mmol) gave, after column chromatography using dichloromethane/hexane (1:3 v/v) as eluant, 1,1-bis(2,6-dibromo-3,5-difluoro-4-pyridyl)ethyl acetate **16** (0.41 g, 23%); mp 158–160 °C; (found: C, 27.0; H, 1.2; N, 4.2. C₁₄H₆Br₄F₄N₂O₂ requires: C, 26.6; H, 0.95; N, 4.4%); δ_{C} 21.4 (s, COCH₃), 26.9 (s, CH₃), 78.14 (s, C–O), 124.3 (X part ABX system, C-2), 128.5 (m, C-4), 153.1 (d, $^1J_{\text{CF}}$ 267, C-3), 168.5 (s, C=O); δ_{H} 2.16 (3H, s, OCOCH₃), 2.34 (3H, s, C–CH₃); δ_{F} –108.05 (s); m/z (EI⁺) 629 (M^+ –H, 0.4), 627 (0.3), 632 (0.2), 587 (5.2), 43 (100%); Cl^- 569 (M^+ –OCOCH₃, 100%).

3.3. X-ray crystallography

Crystal data for 2,6-dibromo-3,5-difluoro(4-pyridyl)methylphenylketone **14**: C₁₃H₇Br₂F₂NO, $M = 391.02$, monoclinic, space group $P2_1/c$, $a = 7.4899(15)$, $b = 22.206(4)$, $c = 8.6648(17)$ Å, $\beta = 113.35(3)^\circ$, $U = 1323.1(5)$ Å³, $F(000) = 752$, $Z = 4$, $D_c = 1.963$ mg m^{–3}, $\mu = 6.14$ mm^{–1} (Mo K α , $\lambda = 0.71073$ Å), $T = 120.0(1)$ K. A 19375 reflections ($1.83 \leq \theta \leq 30.36^\circ$) were collected on a Bruker SMART-CCD diffractometer (ω -scan, 0.3°/frame) yielding 3736 unique data ($R_{\text{merge}} = 0.071$). The structure was solved by direct method and refined by full-matrix least squares on F^2 for all data using SHELXL software [10]. All non-hydrogen atoms were refined with anisotropic displacement parameters, H-atoms were placed at calculated positions and refined using the ‘riding’-mode. Final $wR_2(F^2) = 0.0758$ for all data (172 refined parameters), conventional

$R(F) = 0.0302$ for 3082 reflections with $I \geq 2\sigma$, GOF = 1.047. The largest peak on the residual map is 0.49 a/Å³.

The plane of the carbonyl group in molecule **14** is almost parallel to the plane of heterocycle (corresponding dihedral angle is -10.0°), whilst the dihedral angle between the plane of C=O group and the plane of Ph-ring is -67.2° . The molecules in the stacks are connected by their centres of symmetry and the heterocycles of adjacent molecules overlap with interplanar distances of 3.68 and 3.45 Å. Also there are short intermolecular contacts Br–O 3.054 Å connecting the stacks in *c*-direction.

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