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# $S_{RN}1$ REACTIONS OF CHLOROTRIFLUOROMETHYL PYRIDINES WITH NAPHTHOLATE, PHENOLATE AND MALONATE ANIONS

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***Summary*** *- 2-Chloropyridines, bearing a $CF_3$ group on position 3, 4, 5 or 6 (2-Cl Py $CF_3$) were found to be suitable substrates for photostimulated $S_{RN}1$ reactions with nucleophiles derived from 2-naphthol (Nap-OH) or from phenol (PhOH). Carbon-carbon coupling between the regiospecifically generated 2-pyridyl radical and the carbanionic site of the nucleophile yields 2-heterobiaryl derivatives ($CF_3$Py-Nap-OH or $CF_3$Py-PhOH). Similarly, coupling of the 2-amino-5-$CF_3$.3-pyridyl radical yields 3-heterobiaryl derivatives. Coupling of the malonate anion takes place with the aforementioned radicals.*

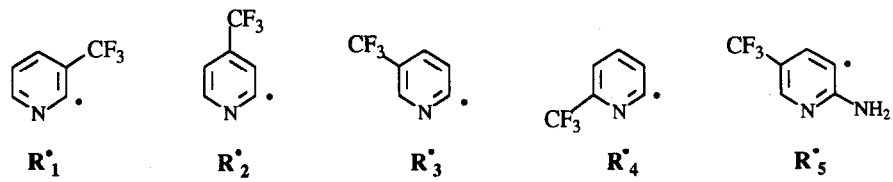
The mechanism[1,2] of the aromatic Radical Nucleophilic Substitution ($S_{RN}1$) reaction is a 4-step chain process described by eq. 1-4.

| | | | | |
|---|---|---|---|---|
| Initiation | ArX | $\xrightarrow{e^-}$ | $ArX^{\cdot -}$ | Eq. 1 |
| Propagation | $ArX^{\cdot -}$ | $\longrightarrow$ | $X^- + Ar^\cdot$ | Eq. 2 |
| | $Ar^\cdot + Nu^-$ | $\longrightarrow$ | $ArNu^{\cdot -}$ | Eq. 3 |
| | $ArNu^{\cdot -} + AX$ | $\longrightarrow$ | $ArNu + ArX^{\cdot -}$ | Eq. 4 |

The activation energy required to promote the monoelectronic transfer to ArX (eq. 1) is usually provided either by photostimulation[2] or by electrocatalysis.[3] A great number of variously substituted substrates are suitable for $S_{RN}1$ reactions with many nucleophiles, so that $S_{RN}1$ chemistry became of large synthetic value[4-6] Recently, we have reported photostimulated reactions leading to fluorinated biaryl derivatives Y-$C_6H_4$.ArOH (Y = F, $CF_3$, $OCF_3$) from Y-$C_6H_4$Br(p) treated with naphtholate for phenolate anions[7] under photostimulation. A very recent paper reporting the electro catalyzed synthesis of a few 4-(trifluoromethylpyridyl)phenols[8] prompted us to publish our study of photostimulated $S_{RN}1$ reactions aimed at providing i) insight into the reactivity of trifluoropyridyl radicals, ii) a general access to new trifluoromethyl pyridyl derivatives .

## RESULTS AND DISCUSSION

Chloropyridines (Cl-Pyr) are known to react smoothly with nucleophiles ($Nu^-$) under $S_{RN}1$ conditions to give regiospecifically substituted products (Pyr-Nu) *via* the intermediates ($ClPyr^{\cdot -}$, $Pyr^\cdot$ and $PyNu^{\cdot -}$).[8] Therefore, our investigation deals with 2-chloropyridines **1a-d** bearing a $CF_3$ group on position 3, 4, 5, 6 and 2-amino-3-chloro-5-trifluoromethyl pyridine **8** which are expected to generate the 2-pyridyl radicals $\mathbf{R^\cdot_1}$, $\mathbf{R^\cdot_2}$, $\mathbf{R^\cdot_3}$, $\mathbf{R^\cdot_4}$ and the 3-pyridyl radical $\mathbf{R^\cdot_5}$.



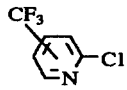
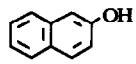
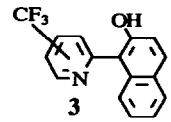
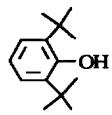
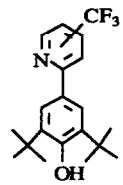
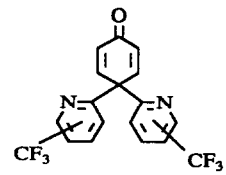
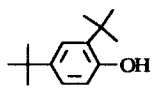
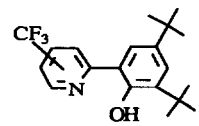
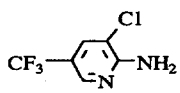
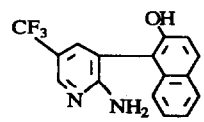
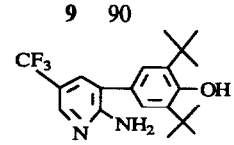
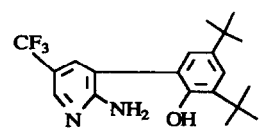
$R^{\bullet}_1$ $R^{\bullet}_2$ $R^{\bullet}_3$ $R^{\bullet}_4$ $R^{\bullet}_5$

Naphtholate and phenolates as nucleophiles (Table 1)

2-Naphthol **2** whose behavior as nucleophile in $S_{RN}1$ reactions is well documented[9,11] gives contrasted results when reacted with **1a-d**. The substrates **1a,b** yield traces of **3a** (entry 1) or no product (entry 2) while **1c** and **1d** lead to the predicted **3c** (entry 3) or **3d** (entry 4) in high (95%) or moderate yield (60%). The low yield of **3a** can be ascribed to steric hindrance of $R^{\bullet}_1$ preventing the approach of the carbanionic site of **2** to give **3a**, substituted on positions adjacent to the heterobiaryl bond by $CF_3$ (ortho) and the 2-hydroxyl of the naphthol. There is no such hindrance to the approach of $R^{\bullet}_2$ whose inertness has to be ascribed to electronic effects induced by 4-$CF_3$ which decreases the electrophilicity of the radical site in meta position. Comparison with the reaction of **1a** treated with **4** (entry 5) shows indeed the importance of steric effect, since $R^{\bullet}_1$ had reacted quite well with a less hindered nucleophile to give **5a** which carries only one substituent ($CF_3$) on position ortho to the bond between the two sub-units. Trace amounts of bis-heteroaryl derivative **5'a** are characterized, resulting from a second $S_{RN}1$ attack of **5a** by **1a**. A similar behavior has been observed in our laboratory from **4** with other fluorinated substrates.[7] The substrate **1c** undergoes an almost quantitative reaction with **4** to give **5c** + **5'c** (97%). When comparing entry 5 to entry 6, one can observe again that $R^{\bullet}_3$ is more reactive than $R^{\bullet}_1$ and by comparing entries 5, 6 to entries 1, 3 respectively, it appears that the less hindered phenolate anion **4** is a better nucleophile than the naphtholate **2**. The anion derived from **6** whose para position is protected by a tert-butyl group undergoes monoarylation only. The reaction with **1b** (entry 7) gives a result consistent with the observed low electrophilicity of the intermediate radical $R^{\bullet}_2$ leading to the formation of **7b**. The result of the reaction of **1c** once more indicates that $R^{\bullet}_3$ is the most reactive trifluoromethyl pyridyl intermediate where the 5-$CF_3$ group enhances the electrophilicity of $R^{\bullet}_3$ without hindering the radical site. The last experiment on 2-trifluoromethyl pyridyl radicals (entry 9) indicates that $R^{\bullet}_4$ generated from **1d** is three times less reactive than $R^{\bullet}_3$ because of the electronic contribution of the 6-$CF_3$ group. The desired product **7d** was nevertheless obtained in high yield after a longer, but still moderate reaction time.

The substrate **8** is the precursor of a structurally more complex 3-pyridyl radical $R^{\bullet}_5$ whose reactivity was anticipated to result from a balance between reverse electronic effects exerted on the radical site by the 5-$CF_3$ and the 2-$NH_2$ groups. When treated with the anion derived from **2**, the substrate **8** gives the heterobiaryl derivative **9** (entry 9). Comparison with entry 1 indicates that the 2-amino group enhances considerably the electrophilicity of the radical site meta to the 5-$CF_3$ group so that the combined effects of the two substituents confer a good reactivity to $R^{\bullet}_5$ The reactions between $R^{\bullet}_5$ and the phenolates from **4** or **6** give contradictory results. The former which reacted efficiently with $R^{\bullet}3$ (entry 6) almost fails to react with $R^{\bullet}_5$ while the latter gives **11** in high yield, consistently with results of entries 8 and 10. Other factors are clearly at work, and further investigations are needed to elucidate the behavior of $R^{\bullet}_5$ towards **4**.

Table 1 $S_{RN}1$ Reactions of **1a-d; 10** with Enolate anions **2, 4, 6**

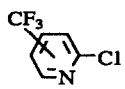
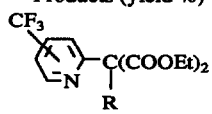
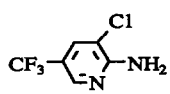
| Entry | Substrate | Nucleophile | Time (min.) | Products (yield %) |
|---|---|---|---|---|
| |  **1** |  **2** | |  **3** |
| 1 | **1a** 3-$CF_3$ | | 240 | **3a** traces |
| 2 | **1b** 4-$CF_3$ | | 240 | **3b** 0 |
| 3 | **1c** 5-$CF_3$ | | 195 | **3c** 95 |
| 4 | **1d** 6-$CF_3$ |  **4** | 240 |   |
| 5 | **1a** 3-$CF_3$ | | 80 | **5a** 66 **5'a** traces |
| 6 | **1c** 5-$CF_3$ | | 45 | **5c** 85 **5'c** 12 |
| | |  **6** | |  |
| 7 | **1b** 4-$CF_3$ | | 240 | **7b** 10 |
| 8 | **1c** 5-$CF_3$ | | 60 | **7c** 98 |
| 9 | **1d** 6-$CF_3$ | | 180 | **7d** 60 (95) |
| |  **8** | **2** | |  |
| 10 | | | 240 | **9** 90 |
| | | | |  |
| 11 | | **4** | 270 | **10** Traces |
| | | | |  |
| 12 | | **6** | 150 | **11** 98 |

Malonates as nucleophiles (Table 2)

It is known from previous studies in our laboratory[12] that a pyridyl radical does not react with malonate except when it bears an electron withdrawing group such as CN. Thus we were led to investigate the reactivity of trifluoromethylpyridyl radicals towards those nucleophiles Results are summarized on Table 2.

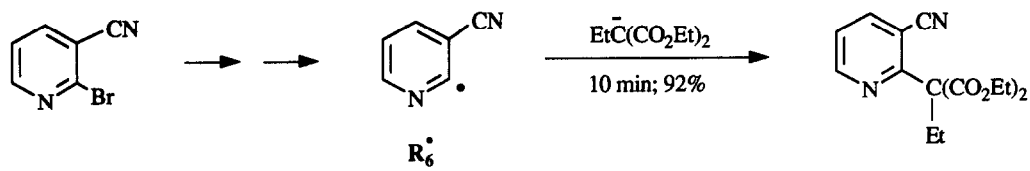
The substrate **1a** reacts neither with the nucleophile derived from **12a** (entry 1) nor with that derived from **12b** (entry 2). In both cases, **1a** is recovered unchanged together with an untractable mixture of products. Thus, the radical $\mathbf{R^{\bullet}_1}$, which reacted with the phenolate **4** to give **5a**, undergoes no reaction with malonate anions in contrast with the highly reactive 3-cyano-2-pyridyl radical derived from the corresponding bromide.

Table 2. $S_{RN}1$ Reactions of **1a-d**; **8** with malonate anions **12a,b**

| Entry | Substrate | Nucleophile | Time (min.) | Products (yield %) |
|---|---|---|---|---|
| |  **1** | $RCH(COOEt)_2$ | |  |
| 1 | **1a** 3-$CF_3$ | **12a** R=H | | **13a** |
| 2 | | **12b** R=Me | | **13b** (a) |
| 3 | **1c** 5-$CF_3$ | **12a** R=H | | **14a** traces |
| 4 | | **12b** R=Me | 15 | **14d** 30 (100) |
| 5 | **1d** 6-$CF_3$ | **12b** R=Me | 240 | **15** 44 (b) |
| 6 |  **8** | **12b** R=Me | 120 | **16** 10 (c) |

a) TLC shows only slow degradation of **1a**. b) Together with 6-trifluoromethylpyridine resulting from competitive reduction of $\mathbf{R_4}$. c) Identified by M.S. $M^+$, m/e = 288.

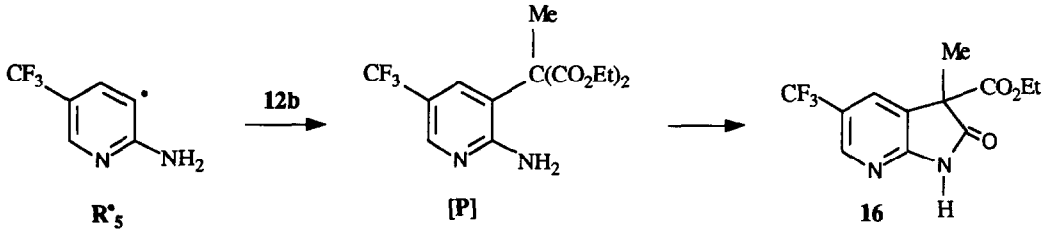
The malonate anion from **12a** reacts very poorly with $\mathbf{R^{\bullet}_3}$ (entry 3) but that from **12b** gives a quantitative yield of **14b** after a short reaction time (entry 4) like a similar tertiary malonate anion reacting with $\mathbf{R^{\bullet}_6}$.[12]




$\mathbf{R^{\bullet}_6}$

Only **12b** was reacted with **1d** to give a mixture of substitution and reduction products. Reduction of radicals is a well documented[13] side reaction in $S_{RN}1$ process, which in the present case gives rise to 6-trifluoromethyl pyridine together with **15**.

The intermediate 3-pyridyl radical $\mathbf{R^{\bullet}_5}$ generated from **8** carries an amino group at position 2 (ortho to the radical) and the primary $S_{RN}1$ product [P] resulting from attack by **12b** is not isolated, because of the




$R^{\bullet}_5$ [P] **16**

spontaneous cyclisation in the strongly alkaline $S_{RN}1$ reaction medium leading to the aza oxindole **16**. Similar "one pot" $S_{RN}1$ reactions with ketone enolates leading to indole[14a-c] or to other heterocycles[4-6] depending upon the nature of the functional group ortho to the radical site are amply precedented. Oxindoles and azaoxindoles have also been obtained by intramolecular $S_{RN}1$ reactions[15a,b] but it is worth noting that the reaction leading to 16 represents an intermolecular access to azaoxindole.

Mechanistic Considerations

Trifluoromethyl pyridines **1a-d** and **8** which were never used before as substrates in $S_{RN}1$ chemistry are indeed reacting by this 4-step mechanism as shown by a series of chemical tests (Table 3) performed on a model reaction between **1c** and the anion derived from **6** .

Table 3

| Conditions | | Time | Product % |
|---|---|---|---|
| **1c** (1 mmol) + **6** (3 mmol) | UV light (entry 8) | 60 min | **7c** 98 |
| | **A** dark | " | 0 |
| | **B** UV light + 1,3-D.N.B.(0.3 mmol) | " | < 1% |
| | **C** UV light + Galvinoxyl (0.1mmol) | " | ~ 20% |

- Under conditions **A** no reaction takes place, a fact clearly demonstrating that activation energy provided by UV light is necessary to promote the monoelectronic transfer to the substrate **1c** leading to the radical anion [**1c**$^{\bullet-}$ (eq. 1].

- Under UV stimulation (eq. 1), but in the presence of a less than stoechiometric amount of 1,3-dinitrobenzene (Conditions **B**), only trace amounts of **7c** are formed while the reaction was complete without DNB for the same reaction time (entry 8). Radical anions **1c**$^{\bullet-}$ and/or **1c**-ArO$^{\bullet-}$ are oxidized by 1,3-DNB to give the *stable* radical anion 1,3 DNB$^{\bullet-}$ which disrupts the chain process described by eq. 1-4.

- Under photostimulation, but in the presence of galvinoxyl (Conditions **C**) the process leading to **7c** does not start until **1c**$^{\bullet}$ which is continuously generated (eq. 1, 2) has consumed all the galvinoxyl. Therefore, after the same reaction time the yield of **7c** is significantly reduced as compared with that of entry 8. Thus, classical experiments **A**, **B**, **C** lend support to the four-step $S_{RN}1$ mechanism *via* ArX$^{\bullet-}$ Ar$^{\bullet}$ and ArNu$^{\bullet-}$ taking place on trifluoro-methylpyridine substrates.

## SCOPE AND LIMITATIONS

The results tabulated in Table 1 and 2 indicate that synthetically useful yields are obtained from **1c** which generates the intermediate radical $\mathbf{R^{\bullet}_3}$. This electrophilic species not subject to steric hindrance undergoes reactions with naphtholate and phenolate anions to give **3c, 5c, 7c** in high yields. The intermediate radical $\mathbf{R^{\bullet}_1}$ is less reactive than $\mathbf{R^{\bullet}_3}$ towards naphtholate and 2,4- tert-butylphenolate because of steric interaction between the $CF_3$ group and the OH of the incoming nucleophile. It is still possible to get reasonable yield of substitution products from **1d** which generates the unhindered but poorly electrophilic radical $\mathbf{R^{\bullet}_4}$, whereas **1b** is not anticipated to be a useful substrate for synthesizing trifluoromethyl heterobiaryl derivatives. The substrate **8** is interesting since it gives heterobiaryl derivatives **9** and **10** in high yield *via* the ortho substituted radical $\mathbf{R^{\bullet}_5}$ and appears to be also a promising substrate for azaoxindole synthesis as evidenced by formation of **16**. A new group of trifluoromethyl heterobiaryl derivatives in addition to fluorobiaryl,[7] heterobiaryl[10] and other variously substituted biaryl compounds[11] becomes thus available by $S_{RN}1$ chemistry.

## EXPERIMENTAL SECTION

Melting points are uncorrected. $^1H$ NMR spectra were recorded at 200 MHz in $CDCl_3$; or MeOD $\delta$ p.p.m. M.S. were obtained by Electronic Impact.

### Procedure for $S_{RN}1$ reactions

In a 100 ml two-necked Pyrex flask containing freshly sublimed *t*-BuOK (3 mmol), ammonia (50 ml) was condensed through a dry ice condenser cooled at -78°C. Under argon atmosphere, the substrate : **1a-d, 8** (1 mmol) and the nucleophile, **2, 4 , 6, 12a,b** (3 mmol) were successively introduced. External irradiation was performed by a high pressure mercury lamp (Hanovia 400 W) and the course of the reaction was monitored by analyzing aliquots. After consumption of the substrate (time), $NH_4Cl$ was added and the solvent was evaporated in a well ventilated hood. Water (100 ml) was then added to the residue and the alkaline solution was extracted with methylene chloride (3 x 50 ml). After classical treatment and evaporation of the organic phase purification was achieved either by silica gel column chromatography (CC, solvent) or preparative layer chromatography (PLC, solvent), and alumina Ad II, III.

### 1-[2-(5-Trifluoromethylpyridyl)]-2-hydroxynaphthalene 3c

(195 min), C.C. pentane/$CH_2Cl_2$, 2/8; M.p. 93°C (pentane), yield 95%, $^1H$ NMR 6.8-8.0 (m, 9H, Ar), 8.80 (b.s. 1H). M.S. m/z 289 ($M^+$). Anal. Calcd for $C_{16}H_{10}F_3NO$ : C, 66.44; H, 3.46. Found: C, 66.37, H, 3.45.

### 1-[2-(6-Trifluoromethylpyridyl)]-2-hydroxynaphthalene 3d

(240 min), P.L.C. heptane:$CH_2Cl_2$, 6/4; M.p. 88°C, (pentane/$CH_2Cl_2$), yield 60%, $^1H$ NMR 7.20-8.20 (m, 9 HAr), 10.2 (s, 1H, OH). M.s. m/z 289 ($M^+$). Anal. Calcd. for $C_{16}H_{10}F_3NO$: C, 66.44, H, 3.46, N, 4.84. Found: C, 66.51, H, 3.66, N, 4.61.

### 1-[2-(3-Trifluoromethylpyridyl)]-3,5-di-t-butyl-4-hydroxybenzene 5a

(80 min), C.C. pentane/$CH_2Cl_2$, 1/1; M.p. 199°C ($CH_2Cl_2$/pentane), yield 66%, $^1H$ NMR 1.5 (s 18H, 2 x t-$C_4H_9$), 7.30 (s, 3H, 7.9-8.0 (d, 1H), 8.8 (d, 1H). M.s. m/z 351 ($m^+$, 336 ($m^+$ - 15). Anal. Calcd for $C_{20}H_{24}F_3NO$: C, 68.38, H, 6.83. Found : C, 68.47, H, 6.58.

**5'a** : M.s. m/z 496 ($m^+$), 481, ($m^+$ - 15).

**1-[2-(5-Trifluoromethylpyridyl)]-4-hydroxybenzene 3,5-di-t-butyl 5c**

(45 min), p.L.C. pentane/$CH_2Cl_2$ 1/1; M.p. 117°C ($CH_2Cl_2$/pentane) lit.[8] 117°C, yield 85%, $^1H$ NMR 1.5 (s, 18H, 2 x t-$C_4H_9$), 7.6-7.9 (m, 4H), 8.8 (b.s., 1H). M.s. m/z 351 ($m^+$), 336 ($m^+$ - 15). Anal. Calcd for $C_{20}H_{24}F_3NO$: C, 68.38, H, 6.83. Found: C, 68.30, H, 6.71.

**5'c.** M.s. m/z 496 ($m^+$), 451, ($m^+$ - 15).

**1-[2-(4-Trifluoromethylpyridyl)]-2-hydroxybenzene 3,5-di-t-butyl 7b**

(240 min), P.L.C., pentane/$CH_2Cl_2$ 6/4; M.p. 97°C ($CHCl_2$/pentane), yield 10%. $^1H$ NMR 1.3 (s, 9H, t-$C_4H_9$), 1.5 (s, 9H, t-$C_4H_9$), 7.25 (b.s., 1H), 7.40 (b.s., 1H), 7.60 (b.s., 1H), 8.05 (b.s., 1H), 8.70 (b.s., 1H). M.s. m/z 351 ($m^+$), 336 ($m^+$ - 15). Anal. Calcd for $C_{20}H_{24}F_3NO$: C, 68.38, H, 6.83, N, 3.99. Found: C, 68.50, H, 6.79, N, 3.76.

**1-[2-(5-Trifluoromethylpyridyl)]-2-hydroxy-3,5-di-t-butylbenzene 7c**

(60 min), C.C. pentane/$CHCl_2$ 6/4; M.p. 105°C (pentane), yield 98%, $^1H$ NMR 1.3 (s, 9H, t-$C_4H_9$), 1.5 (s, 9H, t-$C_4H_9$), 7.35 (d, 1H), 7.55 (d; 1H), 7.9 (bs, 2H), 8.6 (bs, 1H). M.s. m/z 351 ($m^+$), 336 ($m^+$ - 15). Anal. Calcd for $C_{20}H_{24}F_3NO$: C, 68.38, H, 6.38. Found: C, 68.14, H, 6.63.

**1-[2-(6-Trifluoromethylpyridyl)]-2-hydroxy-3,5-di-t-butylbenzene 7d**

(180 min), C.C. alumina ACT II,III, heptane/CH2Cl2 60/40; M.p. 101°C (pentane) of crude product was 95%, but pure **7d** was obtained in 60% yield.
$^1H$ NMR 1.4 (s, 9H, t-C4H9), 1.5 (s, 9H, t-C4H9), 7.47-7.7 (m, 3H), 8.5 (d, 1H), 8.15 (d, 1H), M.s. m/z 351 ($m^+$), 336 ($m^+$ - 15). Anal. Calcd for $C_{20}H_{24}F_3NO$: C, 68.38, H, 6.83, N, 3.99. Found: C, 68.38, H, 7.20, N, 3.88.

**1[3-(2-Amino-4-trifluoromethylpyridyl)]-2-hydroxynaphthalene 9**

(240 min), C.C. $CH_2Cl_2$/MeOH 97/3; M.p. 213-215°C ($CH_2Cl_2$), yield 90%. $^1H$ NMR (MeOD) 7.0-8.0 (m, 7H), 8.6 (b.s. 1H). M.s. m/z 304 ($m^+$), 287. Anal. Calcd for $C_{16}H_{11}F_3N_2O$: C, 63.16, H, 3.62. Found: C, 63.42, H, 3.37.

**1[3-(2-Amino-4-trifluoromethylpyridyl)]-4-hydroxy-3,5-di-t-butylbenzene 10**

(270 min), P.L.C. $CH_2Cl_2$/MeOH 1/99.. M.s. m/z $m^+$ 366, 365, 350.

**1[3-(2-Amino-4-trifluoromethylpyridyl)]-2-hydroxy-3,5-di-t-butylbenzene 11**

(150 min), C.C. $CH_2Cl_2$/MeOH 1/99; M.p. 156-157°C (CH2Cl2), yield 98%. 1H NMR 1.35 (s, 9H, t-C4H9), 1.48 (s, 9H, t-C4H9), 6.90 (d, 1H), 7.35 (d, 1H), 7.55 (d, 1H), 7.9 (b.s. 1H). M.s. m/z 366 ($m^+$), 365, 350. Anal. Calcd for $C_{20}H_{25}F_3N_2O$: C, 65.57, H, 6.83. Found: C, 65.46, H, 6.69.

**2-[2-(5-Trifluoromethylpyridyl)]-malomic acid diethyl ester 14a**

After 60 min, **12a** is consumed bulb to bulb distillation, but **14a** oil was not obtained pure in significant yield. $^1H$ NMR 1.0-1.5 (t, 6H, 2 x $CO_2C_2\underline{CH}CH_3$), 4 - 4.4 (q, 4H, 2 x $CO_2CH_2CO$), 5.05 (s, 1H,

-C<u>H</u>($CO_2CrH_5$), 7.4-7.8 (m, 2H), 8.75 (s, 1H). M.s. m/z 305 ($m^+$), 260 ($m^+$ - 45 : $OC_2H_5$), 233 ($m^+$ - $CO_2C_2H_4$), 187, 161, 14.

**2-[2-(5-Trifluoromethylpyridyl)]-2-methylmalomic acid diethyl ester <u>14d</u>**

(15 min), C.C. pentane/ethyl acetate 1 to 6%); oil. The reaction was complete, but only 30% of pure **14a** was obtained. $^1H$ NMR 1.15-1.4 (t, 6H, 2x $CO_2CH_2$-C<u>H</u>$_3$), 1.90 (s, 3H, C<u>H</u>$_3$), 4.0-4.5 (4H, q, 2 x C<u>H</u>$_2$CH$_3$), 7.4 - 7.9 (m, 2H), 8.65 (b.s., 1H). M.s. m/z 319 ($M^+$). Anal. Calcd for $C_{14}H_{16}F_3NO_4$: C, 52.66; H, 5.02. Found: C, 52.90; H, 4.99.

**2-[2-(6-Trifluoromethylpyridyl)]-2-methyl malomic acid diethyl ester <u>15</u>**

(240 min, P.L.C. heptane/$CH_2Cl_2$ : 1/1), oil, yield 44%, $^1H$ NMR 1.20-1.40 (t, 6H, 2 x $CO_2CH_2$C<u>H</u>$_3$), 1.90 (s, 3H), 4.20 - 4.50 (q, 4H), 7.50 - 8.O (m, 3H). M.s. m/z 319 ($m^+$), 304 ($M^{\pm}15$), 174. Anal. Calcd for $C_{14}F_3NO_4$: C, 52.66; H, H, 5.02. Found: C, 52.40, H, 4.81.

**3-Methyl-3-carboxyclic acid ethyl ester-5-trifluoromethyl-7-aza oxindole <u>16</u>**

(120 min), P.L.C. $CH_2Cl_2$/MeOH 18/2; oil, yield 10%. M.s. m/z 288 ($m^+$).

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