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Naphthalene-catalysed Lithiation of Chlorinated Nitrogenated Aromatic Heterocycles and Reaction with Electrophiles☆

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Abstract—Naphthalene catalysed reductive lithiation of various chloroazines (**1**, **7**, **10**, **13**) in the presence of different electrophiles yields, after hydrolysis, the expected functionalised heterocycles with one (**2**, **8**), two (**11**, **14a–d**) and three nitrogen atoms in the ring (**14e**,**f**). This methodology allowed us to trap in situ the lithium imine derived from the reaction of 2-pyridyllithium with benzonitrile, by reaction with a Grignard reagent in the presence of titanium alkoxides. 2,4-Dimethoxypyrimidines (**14a**,**c**,**d**) are demethylated under acidic conditions to give the corresponding uracil derivatives **16**. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

Nitrogen-containing six-membered aromatic heterocycles are widely represented in nature and play a central role in the field of heterocyclic chemistry.[1] The significance of this chemistry is made clear considering that more than 50% of organic chemistry publications are dedicated to this field, many of the described compounds having a decisive influence in life and society.[2] Many important examples can be found in the word of hereditary information, enzymatic processes, photosynthesis, medicines, as well as other molecules with application in agriculture and industry.[2]

The preparation of nitrogen-containing six-membered aromatic heterocycles derivatives is generally based on the heterocycle itself by substitution at the aromatic ring. One methodology amply developed in the last two decades involves the so-called ortho lithiation of the heterocyclic systems and further reaction with an electrophile.[3] This process, which is well known for π-excessive heterocycles, presents some problems in π-deficient systems for the facile nucleophilic attack of the lithiating reagent (usually an alkyllithium) due to the low-energy level of the corresponding LUMO. Another additional problem of this process has to do, in many cases, with the regiochemistry of the reaction. This difficulty can be overcome using another methodology consisting in a halogen/lithium[4] exchange using *n*-butyllithium as lithiation agent and a brominated[5] or iodinated[6] heterocycle, usually the reaction not being possible for chlorinated derivatives.[7] To the best of our knowledge, the only example described in the literature[8] using a chloropyridine and lithium metal as starting material for the generation of the corresponding organolithium intermediate, required an excess (2:1) of naphthalene. This communication prompted us to apply an arene-catalysed lithiation[9–11] to generate lithiated nitrogen-containing aromatic heterocycles by chlorine/lithium exchange. This methodology has been successfully used in the last few years for the generation of organolithium compounds starting from non-halogenated materials,[9b] functionalised organolithium compounds,[12,13] and polylithiated reagents.[14] The application of this methodology for the lithiation of chlorinated nitrogen-containing heterocycles is described in this paper.

Results and Discussion

The reaction of 2-chloropyridine (**1a**) with an excess of lithium and a substoichiometric amount of naphthalene (4% molar ratio) took place during 1 h at −78°C to lead to the corresponding organolithium **3**, which after addition to pivaldehyde and final hydrolysis, gave the expected alcohol **2a** in 30% isolated yield. This poor yield may be due to the well-known aromatic reduction process in π-deficient azaaromatic compounds.[15] In order to overcome this inconvenience, the whole process was performed under Barbier-type reaction conditions,[16] to give the expected alcohol **2a** in 93% isolated yield (Table 1, entry 1). Other variations tested such as temperature (0°C), amount of lithium (using only the required stoichiometric amount) and electron shuttle (4,4′-di-*tert*-butylbiphenyl), as well as the halopyridine used (2-bromopyridine) decreased the

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Table 1. Preparation of compounds **2**

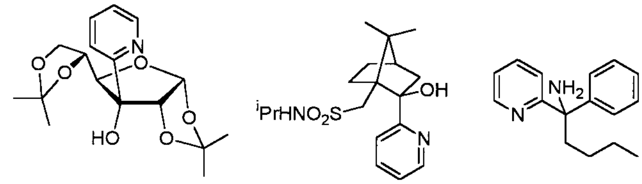
Entry	Starting material	Electrophile (E)	Product		
			No.	X	Yield (%)[a]
1	**1a**	^tBuCHO	**2a**	^tBuCHOH	93
2	**1a**	PhCHO	**2b**	PhCHOH	68
3	**1a**	Et_2CO	**2c**	Et_2COH	64
4	**1a**	PhCOMe	**2d**	PhC(OH)Me	50
5	**1a**	**4**	**2e**	–[b]	35[c]
6	**1a**	**5**	**2f**	–[d]	50[e,f]
7	**1a**	PhCH=CHCOMe	**2g**	PhCH=C(OH)Me	20
8	**1a**	PhCH=NPh	**2h**	PhCHNHPh	25
9	**1a**	**6**	**2i**	$HO(CH_2)_3CO$	10
10	**1a**	$Me(CH_2)_5CON(CH_2)_4$	**2j**	$Me(CH_2)_5CO$	30
11	**1a**	PhCN	**2k**	PhCO	46
12	**1a**	$^iPrO_2CN=NCO_2{}^iPr$	**2l**	$^iPrO_2CNNHCO_2{}^iPr$	20
13	**1b**	^nPrCHO	**2m**	^nPrCHOH	10[g]
14	**1b**	^tBuCHO	**2n**	^tBuCHOH	69
15	**1b**	PhCHO	**2o**	PhCHOH	50[g]
16	**1b**	Et_2CO	**2p**	Et_2COH	58
17	**1b**	PhCOMe	**2q**	PhC(OH)Me	25[g]
18	**1b**	$(n\text{-}C_5H_{11})_2CO$	**2r**	$(n\text{-}C_5H_{11})_2COH$	25
19	**1b**	PhCN	**2s**	PhCO	10[g]
20	**1c**	^tBuCHO	**2t**	^tBuCHOH	74
21	**1c**	Et_2CO	**2u**	Et_2COH	48
22	**1c**	PhCOMe	**2v**	PhC(OH)Me	26

[a] Isolated yield of pure compounds **2** (≥95% from GLC and/or 300 MHz ^1H NMR) after column chromatography (silica gel, hexane/ethyl acetate unless otherwise stated) based on the starting material **1**.
[b] See structure **2e**.
[c] Based on the electrophile used.
[d] See structure **2f**.
[e] Two equivalents of in situ generated 2-pyridyllithium and cerium trichloride were used.
[f] Isolated crude yield.
[g] Basic alumina (hexane/ethyl acetate) was used in the chromatographic purification.

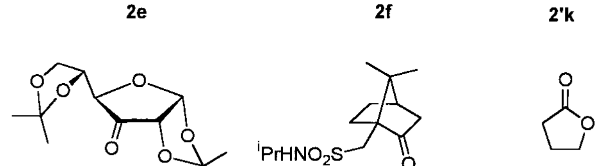
yield of product **2a**. It must be pointed out that when the reaction was carried out in absence of arene, a mixture of di-, tri- and oligoazines was initially formed, which can play the role of electron shuttle for the lithiation reaction,[17] though giving a lower yield (80%) than in the naphthalene-catalysed process.

The reaction of 2-chloropyridine (**1a**) with an excess of lithium and a substoichiometric amount of naphthalene at −78°C, in the presence of various electrophiles led, after hydrolysis with water, to the expected functionalised pyridines **2a–l** (Scheme 1 and Table 1, entries 1–12).

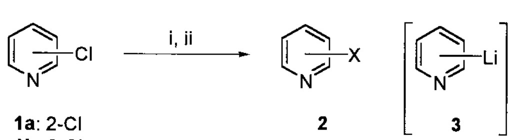
It is worth noting that in the case of using ketones **4** and **5** as electrophiles the reaction took place diastereoselectively, yielding only one of two possible diastereomers **2e** and **2f**, respectively. In the case of the ketone **5**, the reaction was carried out in the presence of anhydrous cerium trichloride[18] and using an extra equivalent of the corresponding pyridyllithium for removal of the active proton of the sulfonamide moiety. When the reaction was performed with benzonitrile (Table 1, entry 11), after hydrolysis, the expected ketone **2k** was isolated. However, this last procedure permitted the trapping of the initially formed lithium imine[19] in a one-pot process simply by adding a solution of butylmagnesium chloride and titanium tetraisopropoxide in toluene, and warming the mixture up to room temperature.[20] Final hydrolysis yielded the expected primary amine **2′k** in a 22% isolated yield.



2e **2f** **2′k**



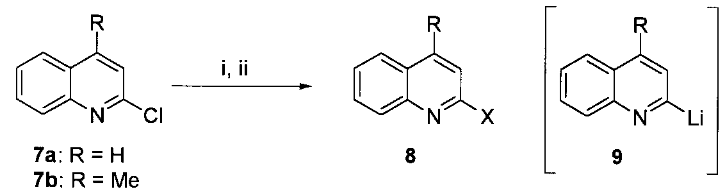
4 **5** **6**



1a: 2-Cl
1b: 3-Cl
1c: 4-Cl

Scheme 1. *Reagents and conditions*: i, Li, $C_{10}H_8$ (4 mol%), E=^nPrCHO, ^tBuCHO, PhCHO, Et_2CO, PhCOMe, $(n\text{-}C_5H_{11})_2CO$, **4**, **5**, PhCH=CHCOMe, PhCH=NPh, **6**, $Me(CH_2)_5CON(CH_2)_4$, PhCN, $^iPrO_2CN=NCO_2{}^iPr$, THF, −78°C; ii, H_2O, −78 to 25°C

When the aforementioned naphthalene-catalysed lithiation process, in the presence of electrophile, was performed with the corresponding 3-chloro and 4-chloropyridines (**1b** and **1c**, respectively), the expected modified pyridines (**2m–v**) were obtained (Scheme 1 and Table 1, entries 13–22).



Scheme 2. *Reagents and conditions*: i, Li, $C_{10}H_8$ (4 mol%), E=^{t}BuCHO, PhCHO, Et_2CO, PhCOMe, THF, −78°C; ii, H_2O, −78 to 25°C

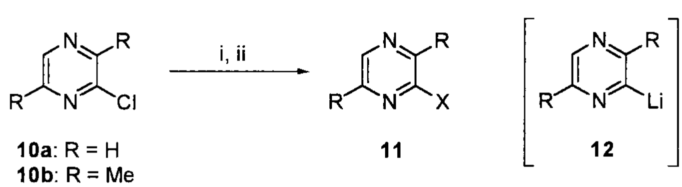
Table 2. Preparation of compounds **8**

Entry	Starting material	Electrophile (E)	Product		
			No.	X	Yield (%)[a]
1	**7a**	^{t}BuCHO	**8a**	^{t}BuCHOH	29 (60)[b]
2	**7a**	PhCHO	**8′b**	PhCO[c]	56
3	**7a**	Et_2CO	**8c**	Et_2COH	21
4	**7a**	PhCOMe	**8d**	PhC(OH)Me	20
5	**7b**	^{t}BuCHO	**8e**	^{t}BuCHOH	25[d] (62)[b]
6	**7b**	Et_2CO	**8f**	Et_2COH	25 (75)[b]

[a] Isolated yield of the compounds **8** (≥94% from GLC and/or 300 MHz ^{1}H NMR) after column chromatography (neutral silica gel, hexane/ethyl acetate, unless otherwise stated) based on the starting material **7**.
[b] Isolated crude yield.
[c] The corresponding secondary alcohol **8b** seems to be unstable under the work-up and purification process, and it is oxidised to the ketone **8′b**.
[d] Basic alumina, hexane/ethyl acetate was used in the chromatographic purification.

The chloroquinolines **7a**,**b** were also submitted to naphthalene-catalysed reductive lithiation at −78°C, in the presence of electrophiles such as aldehydes and ketones, to give, after hydrolysis, the expected quinolines **8** through the corresponding intermediate **9** (Scheme 2 and Table 2). However, it should be pointed out that in the case of using benzaldehyde as electrophile the ketone **8′b** was isolated instead of the expected secondary alcohol **8b**. This alcohol could be identified by GC–MS of the reaction mixture, but it seems to be unstable under the work-up and purification process and was spontaneously oxidised to yield the ketone **8′b**.

Pyrazines **10** were submitted to the naphthalene-catalysed reductive lithiation process under Barbier-type conditions, yielding the expected functionalised pyrazines **11**, the corresponding intermediate **12** being presumably involved in the

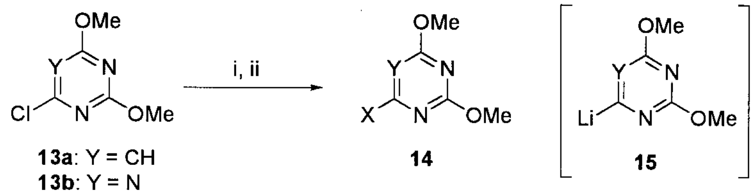


Scheme 3. *Reagents and conditions*: i, Li, $C_{10}H_8$ (4 mol%), E=^{t}BuCHO, PhCHO, Et_2CO, $(CH_2)_5CO$, PhCOMe, PhCH=NPh, PhCN, THF, −78°C; ii, H_2O, −78 to 25°C

Table 3. Preparation of compounds **11**

Entry	Starting material	Electrophile (E)	Product		
			No.	X	Yield (%)[a]
1	**10a**	^{t}BuCHO	**11a**	^{t}BuCHOH	54
2	**10a**	PhCHO	**11b**	PhCHOH	27[b]
3	**10a**	Et_2CO	**11c**	Et_2COH	48
4	**10a**	PhCOMe	**11d**	PhC(OH)Me	30
5	**10b**	^{t}BuCHO	**11e**	^{t}BuCHOH	31[c]
6	**10b**	PhCHO	**11f**	PhCHOH	70[b]
7	**10b**	$(CH_2)_5CO$	**11g**	$(CH_2)_5COH$	38 (60)[d]
8	**10b**	PhCOMe	**11h**	PhC(OH)Me	50[c]
9	**10b**	PhCH=NPh	**11i**	PhCHNHPh	10[c]
10	**10b**	PhCN	**11j**	PhCO	14[c]

[a] Isolated yield of the compounds **11** (≥96% from GLC and/or 300 MHz ^{1}H NMR) after column chromatography (neutral silica gel, hexane/ethyl acetate unless otherwise stated) based on the starting material **10**.
[b] Isolated by acid/base extraction.
[c] Basic alumina, hexane/ethyl acetate was used in the chromatographic purification.
[d] Isolated crude yield.



Scheme 4. *Reagents and conditions*: i, Li, $C_{10}H_8$ (4 mol%), E=^tBuCHO, PhCHO, Me_2CO, Et_2CO, ^iPrCOMe, THF, −78°C; ii, H_2O, −78 to 25°C

Table 4. Preparation of compounds **14**

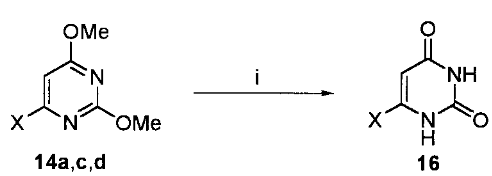
Entry	Starting material	Electrophile (E)	Product No.	X	Yield (%)[a]
1	**13a**	^tBuCHO	**14a**	^tBuCHOH	60
2	**13a**	PhCHO	**14b**	PhCHOH	35[b]
3	**13a**	Et_2CO	**14c**	Et_2COH	45
4	**13a**	^iPrCOMe	**14d**	$^iPrC(OH)Me$	25
5	**13b**	Me_2CO	**14e**	Me_2COH	13
6	**13b**	Et_2CO	**14f**	Et_2COH	50

[a] Isolated yield of the compounds **14** (≥95% from GLC and/or 300 MHz ^1H NMR) after column chromatography (neutral silica gel, hexane/ethyl acetate) based on the starting material **13**.
[b] The reaction was carried out at −30°C.

reaction (Scheme 3 and Table 3). The low isolated yield may be attributed, in some cases, to the unstability of pyrazines **11** under the isolation/purification conditions.

Finally, pyrimidine **13a** and triazine **13b** were lithiated using lithium powder and a substoichiometric amount of naphthalene, in the presence of various electrophiles such as aldehydes and ketones, to give, after hydrolysis, the expected heterocycles **14** (Scheme 4 and Table 4). The reaction presumably takes place through the organolithium intermediate **15**.

In the last part of this study, the transformation of some pyridines **14** into the corresponding 6-substituted uracils **16** was accomplished. Demethylation of compounds **14** was easily performed under standard conditions: reflux of a ca 1:1 mixture of hydrobromic acid (45%) and acetic acid,[21] yielding by crystallization the expected hydroxymethyl substituted uracils **16** as crystalline solids (Scheme 5 and Table 5).



Scheme 5. *Reagents and conditions*: i, 45% HBr, glacial AcOH, reflux

Table 5. Preparation of compounds **16**

Entry	Starting pyrimidine	Product No.	X	Yield (%)[a]
1	**14a**	**16a**	^tBuCHOH	90
2	**14c**	**16b**	Et_2COH	32
3	**14d**	**16c**	$^iPrC(OH)Me$	51

[a] Isolated crude yield of the pure compounds **16** (≥90% from 300 MHz ^1H NMR) based on the starting material **14**.

Conclusion

In conclusion, we have described here a simple method for the preparation of lithiated nitrogen aromatic heterocycles by a naphthalene-catalysed chlorine–lithium reductive exchange. These organolithium derivatives allow the preparation of various fuctionalised nitrogen-containing six-membered aromatic heterocycles. In the case of alkoxypyrimidine derivatives, these compounds may be used to prepare 6-substituted uracils.

Experimental

General

For general information see Ref. 18.

Naphthalene-catalysed lithiation of chloroazines 1, 7, 10 and 13 in the presence of electrophiles

*Isolation of compounds **2**, **8**, **11** and **14**. General procedure*—to a green suspension of lithium powder (50 mg, 7 mmol) and naphthalene (20 mg, 0.16 mmol) in THF (5 mL) was slowly added (ca 10 min) a solution of the corresponding azine **1**, **7**, **10** or **13** (2 mmol) and the electrophile (2.5 mmol) in THF (2 mL) at −78°C under an argon atmosphere. Stirring was continued at the same temperature until no starting azine was detected by GC (from 0.5 to 5 h). The resulting mixture was then hydrolysed with water (5 mL) and extracted with ethyl acetate (2×20 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvents were evaporated (15 Torr) to give a residue, which was purified in general by column chromatography (see, footnotes in Tables 1–4) affording the pure title compounds. Yields are included in Tables 1–4. Physical, spectroscopic and analytical data, as well as the literature reference for the known compounds, follow:

2,2-Dimethyl-1-(pyrid-2-yl)propan-1-ol (2a).[22] Colourless oil, t_r 9.6; R_f 0.52 (hexane/ethyl acetate: 1:1); ν (film) 3386 (OH), 3088, 3064, 1595 (HC═C), 1063 cm^{-1} (CO); δ_H ($CDCl_3$) 0.90 (9H, s, 3×CH_3), 4.35 (1H, s, C*H*OH), 4.46 (1H, s, OH), 7.15–7.65, 8.48 (3 and 1H, respectively, m, and d, respectively, *J*=4.9 Hz, ArH); δ_C ($CDCl_3$) 25.6 (3C), 35.75, 80.15, 121.9, 122.45, 135.25, 147.3, 160.2; *m/z* 166 (M^++1, <1%), 150 (M^+−CH_3, 1), 109 (100), 79 (21), 78 (17), 53 (11), 52 (11), 41 (16).

1-Phenyl-1-(pyrid-2-yl)methanol (2b).[23] Pale yellow oil, t_r 13.4; R_f 0.70 (ethyl acetate); ν (film) 3350 (OH), 3060, 3028, 1593 (HC═C), 1051, 1026 cm^{-1} (CO); δ_H ($CDCl_3$) 5.49 (1H. s, OH), 5.73 (1H, s, C*H*OH), 7.10–7.60, 8.46 (8 and 1H, respectively, m, and d, respectively, *J*=4.3 Hz, ArH); δ_C ($CDCl_3$) 75.0, 121.1, 122.2 (2C), 126.8, 127.5, 128.35 (2C), 136.7, 143.05, 147.7, 161.1; *m/z* 186 (M^++1, 4%), 185 (M^+, 34), 184 (20), 108 (34), 105 (11), 80 (31), 79 (100), 78 (43), 77 (40), 53 (13), 52 (33), 51 (41), 50 (14), 44 (12).

3-(Pyrid-2-yl)pentan-3-ol (2c). t_r 8.7; R_f 0.20 (hexane/ethyl acetate: 1:1); ν (film) 3327 (OH), 3033, 1605 (HC═C), 1150 cm^{-1} (CO); δ_H ($CDCl_3$) 0.68 (6H, t, *J*=7.4 Hz, 2×CH_3), 1.65–2.05 (4H, m, 2×CH_2), 5.28 (1H, s, OH), 7.15–7.30, 7.65–7.75, 8.50–8.55 (1, 2 and 1H, respectively, 3m, ArH); δ_C ($CDCl_3$) 7.7 (2C), 34.65 (2C), 76.4, 119.6, 121.55, 136.75, 147.05, 163.35; *m/z* 150 (M^+−CH_3, 2%), 137 (17),136 (100), 118 (25), 117 (22), 80 (21), 79 (24), 78 (16), 53 (13), 52 (23), 51 (17); HRMS: M^+−CH_3, found 150.0917. $C_9H_{12}NO$ requires 150.0919.

1-Phenyl-1-(pyrid-2-yl)ethanol (2d).[24] Pale yellow oil, t_r 13.2; R_f 0.59 (hexane/ethyl acetate: 1:1); ν (film) 3385 (OH), 3087, 3059, 1591 (HC═C), 1062 cm^{-1} (CO); δ_H ($CDCl_3$) 1.91 (3H, s, CH_3), 5.85 (1H, s, OH), 7.10-7.65, 8.47 (8, and 1H, respectively, m and d, respectively, *J*=4.8 Hz, ArH); δ_C ($CDCl_3$) 29.05, 74.95, 120.15, 121.85, 125.75, 126.8 (2C), 128.05 (2C), 136.85, 147.0, 147.25, 164.6; *m/z* 200 (M^++1, 9%), 199 (M^+, 66), 184 (47), 180 (23), 156 (15), 122 (47), 121 (11), 106 (30), 105 (22), 104 (14), 91 (16), 80 (34), 79 (85), 78 (74), 77 (40), 52 (30), 51 (40), 50 (12), 43 (100).

1,2:5,6-Di-*O*-isopropyliden-3-(pyrid-2-yl)-α-D-allofuranose (2e).[5c,25] White solid, mp 129–131°C (ethyl acetate/hexane); t_r 16.3; R_f 0.70 (hexane/ethyl acetate: 1:1); $[\alpha]_D^{25}$=+61.4 (*c* 1.9, CH_3COCH_3); ν (melted) 3472 (OH), 3059, 1591 (HC═C), 1071 cm^{-1} (CO); δ_H ($CDCl_3$) 1.18 (3H, s, CH_3), 1.38 (3H, s, CH_3), 1.40 (3H, s, CH_3), 1.65 (3H, s, CH_3), 3.20–3.25 (1H, m, C*H*CH_2), 3.55–3.60 (2H, m, CH_2), 3.79 (1H, s, OH), 4.23 (1H d, *J*=5.5 Hz, C*H*CHCH_2), 4.66 (1H, d, *J*=3.7 Hz, C*H*CHO_2), 6.15 (1H, d, *J*=3.7 Hz, OCHO), 7.20–7.25, 7.65–7.75, 8.52 (1, 2 and 1H, respectively, 2m and d, respectively, *J*=4.9 Hz, ArH); δ_C ($CDCl_3$) 25.0, 26.2, 26.3, 26.7, 65.35, 73.55, 81.5, 83.15, 83.65, 105.5, 108.45, 112.2 (2C), 121.1, 122.5, 136.0, 147.9, 158.45; *m/z* 338 (M^++1, <1%), 337 (M^+, <1), 322 (43), 279 (13), 236 (12), 220 (16), 207 (30), 204 (18), 178 (10), 164 (10), 162 (17), 150 (27), 149 (100), 148 (15), 132 (11), 131 (18), 122 (16), 121 (74), 120 (28), 106 (24), 104 (13), 101 (20), 100 (29), 93 (53), 92 (12), 85 (21), 80 (11), 79 (57), 78 (55), 65 (10), 59 (44), 52 (17), 51 (12), 43 (68), 42 (19), 41 (22).

(1*S*,2*R*,4*S*)-*N*-Isobutyl-2-hydroxy-7,7-dimethyl-2-(pyrid-2-yl)bicyclo[2.2.1]hept-1-ylmethanesulfonamide (2f).[26] Pale yellow oil, t_r 14.3; R_f 0.4 (hexane/ethyl acetate: 7:3); $[\alpha]_D^{25}$=+80.3 (*c* 0.1, CH_2Cl_2); ν (film) 3404 (OH,NH), 1593 (HC═C), 1139 (CO), 1076 cm^{-1} (SO); δ_H ($CDCl_3$) 0.95[6H, d, *J*=6.7 Hz, (C*H*$_3$)$_2$CH], 1.05 (3H, s, CH_3C), 1.30 (3H, s,CH_3), 1.45–2.00 [8H, m, $CH_2CH_2CHCH_2$, C*H*(CH_3)$_2$], 2.75–2.95 (2H, m, C*H*$_2$NH), 2.97, 3.70 (1 and 1H, respectively, 2d, *J*=15.3 Hz, CH_2S), 4.80 (1H, m, NH), 6.01 (1H, s, OH), 7.25–7.75, 8.50–8.55 (3 and 1H, respectively, 2m, ArH); δ_C ($CDCl_3$) 19.95 (2C), 21.55 (2C), 26.45, 27.2, 28.85, 44.75, 47.6, 50.25, 50.7, 53.2, 55.1, 82.05, 111.55, 122.15, 122.6, 136.65, 146.6; *m/z* 331 (M^+−35, <1%), 201 (11), 160 (17), 146 (25), 122 (37), 121 (29), 108 (31), 107 (10), 106 (21), 93 (95), 91 (11), 80 (14), 79 (75), 78 (100), 67 (20), 55 (14), 53 (20), 52 (18), 51 (27), 44 (18), 43 (17), 41 (60).

(*E*)-4-Phenyl-2-(pyrid-2-yl)-3-buten-2-ol (2g).[25,27] White solid, mp 106–108°C (ethyl acetate/hexane); t_r 15.5; R_f 0.49 (hexane/ethyl acetate: 1:1); ν (film) 3256 (OH), 3084, 3055, 1590 (HC═C), 1180 cm^{-1} (CO); δ_H ($CDCl_3$) 1.72 (3H, s, CH_3), 5.55 (1H, s, OH), 6.46 (1H, d, *J*=15.9 Hz, CHCO), 6.73 (1H, d, *J*=15.9 Hz, C*H*CHCO), 7.15–7.70, 8.50–8.55 (8 and 1H, respectively, 2m, ArH); δ_C (CD_3COCD_3) 29.7, 75.1, 120.45, 122.75 (2C), 127.2 (2C), 127.5, 128.0, 129.3 (2C), 137.65, 137.80, 148.6, 165.9; *m/z* 226 (M^++1, <1%), 225 (M^+, 3), 209 (17), 208 (100), 207 (19), 206 (26), 182 (25), 122 (13), 106 (17), 104 (36), 102 (11), 79 (23), 78 (44), 77 (17), 52 (14), 51 (21), 43 (33).

***N*-Phenyl-*N*-[1-phenyl-1-(pyrid-2-yl)]methylamine (2h).**[28] Yellow oil, t_r 17.8; R_f 0.49 (hexane/ethyl acetate: 4:1); ν (film) 3392 (NH), 3052, 3024, 1601 cm^{-1} (HC═C); δ_H ($CDCl_3$) 5.50 (1H, s, NH), 5.55 (1H, s, C*H*NH), 6.60–6.65, 7.05–7.40, 8.50–8.55 (3, 10 and 1H, respectively, 5m, ArH); δ_C ($CDCl_3$) 63.0, 113.4 (3C), 117.2, 121.65, 121.95, 127.15 (2C), 128.6 (2C), 128.9 (2C), 136.6, 142.3, 146.8, 148.9, 160.6; *m/z* 261 (M^++1, 9%), 260 (M^+, 46), 183 (29), 182 (100), 169 (13), 168 (91), 167 (60), 166 (10), 104 (13), 78 (10), 77 (37), 51 (21).

4-Hydroxy-1-(pyrid-2-yl)-1-butanone (2i). Pale yellow oil, t_r 8.8; R_f 0.49 (ethyl acetate); ν (film) 3372 (OH), 1584 (HC═C), 1696 (C═O), 1044 cm^{-1} (CO); δ_H ($CDCl_3$) 2.00–2.10 (2H, m, CH_2C*H*$_2$$CH_2$), 2.49 (1H, m, OH), 3.33 (2H, t, *J*=6.7 Hz, CH_2C═O), 3.70–3.75 (2H, m, CH_2O), 7.45–8.05, 8.65–8.70 (3 and 1H, respectively, 2m, ArH); δ_C ($CDCl_3$) 27.65, 34.25, 62.0, 121.85, 127.25, 137.1, 148.85, 153.4, 202.45; *m/z* 166 (M^++1, <1%), 165 (M^+, 2), 134 (48), 122(16), 121 (13), 118 (11), 107 (16), 106 (30), 93 (24), 80 (20), 79 (100), 78 (99), 55 (11), 53 (11), 52 (50), 51 (58), 50 (17), 43 (13), 41 (22); HRMS: M^+, found 165.0790. $C_9H_{11}NO_2$ requires 165.0789.

1-(Pyrid-2-yl)heptan-1-one (2j).[29] Colourless oil, t_r 12.2; R_f 0.73 (hexane/ethyl acetate: 7:3); ν (film) 3054, 3007, 1584 (HC=C), 1697 cm^{-1} (C=O); δ_H ($CDCl_3$) 0.89 (3H, t, J=2.1 Hz, CH_3), 1.30–1.40, 1.65–1.80 [6 and 2H, respectively, 2m, $CH_3(CH_2)_4$], 3.21 (2H, t, J=7.3 Hz, CH_2C=O), 7.40–8.05, 8.65–8.70 (3 and 1H, respectively, 2m, ArH); δ_C ($CDCl_3$) 13.9, 22.4, 23.8, 28.9, 31.55, 37.55, 121.6, 126.8, 136.7, 148.75, 153.45, 202.05; m/z 192 (M^++1, 3%), 191 (M^+, 12), 148 (14), 135 (14), 134 (56), 122 (10), 121 (22), 120 (32), 109 (14), 107 (16), 106 (53), 93 (27), 80 (20), 79 (100), 78 (85), 55 (11), 52 (25), 51 (32), 43 (36), 41 (37).

Phenyl pyrid-2-yl ketone (2k).[30] Pale yellow oil, t_r 13.3; R_f 0.53 (hexane/ethyl acetate: 7:3); ν (film) 3056, 1597 (HC=C), 1668 cm^{-1} (C=O); δ_H ($CDCl_3$) 7.40–8.10, 8.65–8.70 (8 and 1H, respectively, 2m, ArH); δ_C ($CDCl_3$) 124.35, 125.95, 127.9 (2C), 130.75 (2C), 132.65, 136.05, 136.85, 148.3, 154.8, 193.55; m/z 184 (M^++1, 4%), 183 (M^+, 29), 182 (55), 155 (86), 154 (36), 105 (85), 78 (20), 77 (100), 52 (12), 51 (66), 50 (21).

Isopropyl 2-(pyrid-2-yl)-3-isopropoxycarbonylcarbazate (2l).[26] Pale yellow oil, t_r 14.8; R_f 0.72 (ethyl acetate); ν (film) 3309 (NH), 1727 (C=O), 1594 (HC=C), 1105 cm^{-1} (CO); δ_H ($CDCl_3$) 1.25–1.35 (12H, m, 4×CH_3), 4.95–5.10 [2H, m, 2×$CH(CH_3)_2$], 7.05–7.10, 7.60–7.80, 8.35–8.40, (1, 2, 1H, respectively, 3m, ArH); δ_C ($CDCl_3$) 21.8 (4C), 69.6, 70.85 (2C), 118.5, 120.7, 137.6, 147.6, 155.75, 153.2, 153.95; m/z 237 (M^+−44, <1%), 135 (62), 109 (38), 108 (20), 80 (11), 79 (23), 43 (100), 41 (33).

1-(Pyrid-3-yl)butan-1-ol (2m).[31] Pale yellow oil, t_r 10.4; R_f 0.31 (ethyl acetate); ν (film) 3373 (OH), 1594 (HC=C), 1026 cm^{-1} (CO); δ_H ($CDCl_3$) 0.94 (3H, t, J=7.3 Hz, CH_3), 1.30–1.80 (4H, 1m, 2×CH_2), 2.73 (1H, s, OH), 4.70–4.75 (1H, m, CHO), 7.25–7.30, 7.65–7.70, 8.45–8.50, (1, 1 and 2H, respectively, 3m, ArH); δ_C ($CDCl_3$) 13.85, 18.8, 41.2 (2C), 71.85, 123.45, 133.6, 147.75 (2C), 148.6; m/z 152 (M^++1, <1%), 151 (M^+, 6), 108 (100), 80 (35), 78 (11), 53 (18), 51 (12).

2,2-Dimethyl-1-(pyrid-3-yl)propan-1-ol (2n).[32] Colourless oil, t_r 9.9; R_f 0.45 (ethyl acetate); ν (film) 3409 (OH), 1605 (HC=C), 1064, 1015 cm^{-1} (CO); δ_H ($CDCl_3$) 0.93 (9H, s, 3×CH_3), 4.35–4.45 (1H, m, CHO), 4.85–4.95 (1H, m, OH), 7.20–7.30, 8.45–8.55 (2 and 2H, respectively, 2m, ArH); δ_C ($CDCl_3$) 25.65 (3C), 35.7, 79.95, 120.45, 122.7, 135.15, 148.4, 149.55; m/z 166 (M^++1, <1%), 165 (M^+, 1), 109 (100), 108 (73), 80 (21), 78 (11), 57 (35), 53 (21), 52 (11),51 (17).

1-Phenyl-1-(pyrid-3-yl)methanol (2o).[23] Colourless oil, t_r 13.9; R_f 0.17 (hexane/ethyl acetate: 1:2); ν (film) 3408 (OH), 1594 (HC=C), 1021 cm^{-1} (CO); δ_H ($CDCl_3$) 4.65 (1H, s, OH), 5.86 (1H. s, CHO), 7.25–8.45, 8.56 (8 and 1H, respectively, m and d, respectively, J=1.8 Hz, ArH); δ_C (CD_3OD) 74.5, 125.0, 127.5 (2C), 128.5, 129.5 (2C), 136.5, 142.5, 145.0, 148.55, 148.7; m/z 186 (M^++1, 6%), 185 (M^+, 44), 184 (20), 108 (12), 107 (14), 106 (37), 105 (24), 80 (85), 79 (100), 78 (63), 77 (45), 53 (17), 52 (23), 51 (51), 50 (17).

3-(Pyrid-3-yl)pentan-3-ol (2p).[33] Pale yellow oil, t_r 9.6; R_f 0.18 (hexane/ethyl acetate: 1:1); ν (film) 3259 (OH), 3045, 1604 (HC=C), 1161 cm^{-1} (CO); δ_H ($CDCl_3$) 0.76, 0.78 (7H, 2t and 1s, J=7.3 Hz, 2×CH_3, OH), 1.80–1.95 (4H, m, 2×CH_2), 7.20–7.30, 7.70–7.80, 8.45–8.65 (1, 1 and 2H, respectively, 3m, ArH); δ_C ($CDCl_3$) 7.6, 7.65, 34.8, 34.95, 76.15, 120.9, 122.9, 147.4, 147.5, 149.4; m/z 165 (M^+, <1%), 136 (100), 94 (45), 93 (17), 78 (15), 57 (26), 51 (23), 43 (37).

1-Phenyl-1-(pyrid-3-yl)ethanol (2q).[34] Pale yellow oil, t_r 13.9; R_f 0.48 (ethyl acetate); ν (film) 3205 (OH), 3085, 3058, 1597 (HC=C), 1207 cm^{-1} (CO); δ_H ($CDCl_3$) 1.91 (3H, s, CH_3), 4.50 (1H, s, OH), 7.15–7.75, 8.25–8.30, 8.49 (7, 1 and 1H, respectively, 2m and d, respectively, J=1.8 Hz, ArH); δ_C ($CDCl_3$) 30.5, 74.5, 120.9, 123.0, 125.75 (3C), 127.05, 128.2, 133.9, 143.95, 147.25, 149.0; m/z 200 (M^++1, 1%), 199 (M^+, 5), 185 (13), 184 (100), 121 (13), 106 (73), 79 (27), 78 (43), 77 (32), 51 (35), 50 (11), 43 (88).

6-(Pyrid-3-yl)undecan-6-ol (2r).[35] Pale yellow oil, t_r 15.1; R_f 0.54 (hexane/ethyl acetate: 1:1); ν (film) 3380 (OH), 3046, 1576 (HC=C), 1026 cm^{-1} (CO); δ_H ($CDCl_3$) 0.82 (6H, t, J=6.7 Hz, 2×CH_3), 1.20–1.25, 1.75–1.85 (12 and 4H, respectively, 2m, 8×CH_2), 2.36 (1H, s, OH), 7.20–7.25, 7.70–7.75, 8.40–8.45, 8.61 (1, 1, 1 and 1H, respectively, 3m and d, respectively, J=1.8 Hz, ArH); δ_C ($CDCl_3$) 13.95 (2C), 22.45 (2C), 23.0 (2C), 32.1 (2C), 42.85 (2C), 75.8, 122.9, 133.3, 147.2, 147.35, 149.35; m/z 231 (M^+-H_2O, <1%), 179 (12), 178 (100), 106 (15), 43 (17), 41 (22).

Phenyl pyrid-3-yl ketone (2s).[30] Pale yellow oil, t_r 13.4; R_f 0.67 (ethyl acetate); ν (film) 3059, 1584 (HC=C), 1662 cm^{-1} (CO); δ_H ($CDCl_3$) 7.45–7.65, 7.80–7.85, 8.10–8.15, 8.80–8.85, 8.95–9.00 (4, 2, 1, 1 and 1H, respectively, 5m, ArH); δ_C ($CDCl_3$) 123.5, 128.55 (2C), 130.0 (2C), 133.1, 137.1, 150.9 (2C), 152.8 (2C); m/z 184 (M^++1, 9%), 183 (M^+, 66), 182 (26), 106 (23), 105 (100), 78 (38), 77 (91), 51 (78), 50 (27).

2,2-Dimethyl-1-(pyrid-4-yl)propan-1-ol (2t).[36] Pale yellow oil, t_r 7.4; R_f 0.33 (ethyl acetate); ν (film) 3376 (OH), 1644 (HC=C), 1064, cm^{-1} (CO); δ_H ($CDCl_3$) 0.92 (9H, s, 3×CH_3), 1.25 (1H, s, OH), 4.35 (1H, s, CHO), 7.25, 8.48 (2 and 2H, respectively, 2d, J=5.8 Hz, ArH); δ_C ($CDCl_3$) 25.7 (3C), 35.5, 80.85, 122.85 (2C), 148.8 (2C), 151.3; m/z 165 (M^+, <1%), 110 (100), 109 (22), 57 (36), 43 (12), 41 (37).

3-(Pyrid-4-yl)pentan-3-ol (2u).[37] Pale yellow oil, t_r 9.9; R_f 0.41 (ethyl acetate); ν (film) 3409 (OH), 1605 (HC=C), 1161 cm^{-1} (CO); δ_H ($CDCl_3$) 0.76 (6H, t, J=7.3 Hz, 2×CH_3), 1.75–1.85 (4H, m, 2×CH_2), 1.88 (1H, s, OH), 7.30, 8.55 (2 and 2H, respectively, 2d, J=6.1 Hz, ArH); δ_C ($CDCl_3$) 7.5 (2C), 34.8 (2C), 76.8, 120.9 (2C), 149.5 (2C), 155.05; m/z 166 (M^++1, <1%), 165 (M^+, <1), 136 (100), 94 (61), 79 (11), 78 (13), 57 (37), 52 (11), 51 (26), 43 (39).

1-Phenyl-1-(pyrid-4-yl)ethanol (2v).[34] White solid, mp 117–118°C (ethyl acetate/hexane) (lit.[34] 146–148°C); t_r 14.4; R_f 0.41 (ethyl acetate); ν (melted) 3159 (OH), 3084, 3054, 1598 (HC=C), 1221 cm^{-1} (CO); δ_H ($CDCl_3$) 1.91 (3H, s, CH_3), 2.58 (1H, s, OH), 7.25–7.50, 8.37 (7 and 2H, respectively, m and d, respectively, J=6.1 Hz, ArH); δ_C (CD_3OD) 30.1, 75.85, 122.7 (2C), 123.1, 127.0 (2C), 128.2, 129.3 (2C), 149.8 (2C), 160.5; m/z 200 (M^++1, 1%), 199 (M^+, 6), 185 (11), 184 (80), 121 (29), 106 (58), 105 (12), 79 (50), 78 (39), 77 (29), 51 (43), 50 (13), 43 (100).

2,2-Dimethyl-1-(quinol-2-yl)propan-1-ol (8a).[25,38] Pale yellow solid, mp 58–60°C (ethyl acetate/hexane); t_r 14.3; R_f 0.62 (hexane/ethyl acetate: 7:3); ν (melted) 3415 (OH), 3061, 3046, 1601 (HC=C), 1063, 1016 cm^{-1} (CO); δ_H ($CDCl_3$) 0.98 (9H, s, 3×CH_3), 4.52, 4.83 (1 and 1H, respectively, 2d, J=6.7 Hz, CHOH), 7.35–7.85, 8.07 (4 and 2H, respectively, m and d, respectively, J=8.5 Hz, ArH); δ_C ($CDCl_3$) 26.05 (3C), 36.65, 80.45, 120.9 (2C), 126.2, 127.4, 128.85, 129.45, 135.25, 146.4, 160.55; m/z 216 (M^++1, <1%), 159 (64), 158 (100), 130 (13), 129 (14), 128 (30), 77 (11), 41 (15).

Phenyl quinol-2-yl ketone (8′b).[25,39] White solid, mp 97–99°C (ethyl acetate/hexane); t_r 17.1; R_f 0.71 (hexane/ethyl acetate: 7:3); ν (KBr) 3442 (OH), 3055, 3023, 1663 (HC=C), 1168 cm^{-1} (CO); δ_H ($CDCl_3$) 7.50–8.25, 8.35 (10 and 1H, respectively, m and d, respectively, J=8.5 Hz, ArH); δ_C ($CDCl_3$) 120.7, 127.6, 128.1 (2C), 128.35 (2C), 128.8, 130.0, 130.45, 131.4, 133.0, 136.1, 137.0, 146.7, 154.65, 193.7; m/z 234 (M^++1, 8%), 233 (M^+, 45), 232 (35), 206 (11), 205 (70), 204 (88), 105 (68), 101 (17), 77 (100), 75 (13), 51 (40), 50 (16).

3-(Quinol-2-yl)pentan-3-ol (8c). Pale yellow oil, t_r 14.0; R_f 0.55 (hexane/ethyl acetate: 7:3); ν (film) 3404 (OH), 3059, 1601 (HC=C), 1159 cm^{-1} (CO); δ_H ($CDCl_3$) 0.69 (6H, t, J=8.5 Hz, 2×CH_3), 1.80–2.05 (4H, m, 2×CH_2), 5.84 (1H, s, OH), 7.35–8.15 (6H, m, ArH); δ_C ($CDCl_3$) 7.75 (2C), 34.35 (2C), 76.6, 117.4 (2C), 126.3, 128.8 (2C), 129.65, 137.05, 145.7, 163.4; m/z 200 (M^+−CH_3, 1%), 187 (24), 186 (100), 168 (18), 167 (20), 130 (33), 129 (19), 128 (13); HRMS: M^+−CH_3, found 200.1069. $C_{13}H_{14}NO$ requires 200.1075.

1-Phenyl-1-(quinol-2-yl)ethanol (8d).[40] Pale yellow solid, mp 95–97°C (ethyl acetate/hexane) (lit. 102°C); t_r 17.2; R_f 0.70 (hexane/ethyl acetate: 7:3); ν (KBr) 3340 (OH), 3059, 3024, 1597 (HC=C), 1126 cm^{-1} (CO); δ_H ($CDCl_3$) 2.00 (3H, s, CH_3), 6.69 (1H, s, OH), 7.20–8.15 (11H, m, ArH); δ_C ($CDCl_3$) 28.6, 75.0, 118.45, 126.25 (2C), 126.6 (2C), 127.1, 127.15, 127.4, 128.25, 128.8, 129.9, 137.25, 145.5, 146.4, 164.3; m/z 250 (M^++1, 12%), 249 (M^+, 55), 234 (34), 230 (12), 172 (46), 128 (58), 102 (19), 101 (16), 77 (32), 51 (20), 43 (100).

2,2-Dimethyl-1-(4-methylquinol-2-yl)propan-1-ol (8e). Yellow solid, mp 81–79°C (ethyl acetate/hexane); [Found: C, 78.15; H, 8.34; N, 5.93. $C_{15}H_{19}NO$ requires C, 78.56, H, 8.35, N, 6.11%]; t_r 15.2; R_f 0.40 (hexane/ethyl acetate: 1:1); ν (melted) 3404 (OH), 3065, 1602 (HC=C), 1073 cm^{-1} (CO); δ_H ($CDCl_3$) 0.98 (9H, s, 3×CH_3), 2.71 (3H, s, CH_3Ar), 4.47 (1H, s, CHO), 4.85 (1H, s, OH), 7.15–8.00, 8.07 (4 and 1H, respectively, m and d, respectively, J=7.3 Hz, ArH); δ_C ($CDCl_3$) 18.9, 26.15(3C), 36.7, 80.3, 121.65, 123.65, 126.0, 127.5, 129.15, 129.5, 143.4 (2C), 160.2; m/z 214 (M^+−CH_3, 2%), 173 (46), 172 (100), 143 (12), 142 (14), 115 (12), 41 (11).

3-(4-Methylquinol-2-yl)pentan-3-ol (8f). Pale yellow oil, t_r 14.9; R_f 0.49 (hexane/ethyl acetate: 7:3); ν (film) 3384 (OH), 3061, 1603 (HC=C), 1163 cm^{-1} (CO); δ_H ($CDCl_3$) 0.69 (6H, t, J=7.3 Hz, 2×CH_3CH_2), 1.80–2.05 (4H, m, 2×CH_2), 2.70 (3H, s, CH_3Ar), 5.90 (1H, s, OH), 7.15–8.00, 8.07 (4 and 1H, respectively, m and d, respectively, J=8.5 Hz, ArH); δ_C ($CDCl_3$) 7.7 (2C), 19.0, 34.25 (2C), 76.35, 117.8, 123.55 126.0, 128.6, 129.2, 129.25, 145.15, 145.4, 162.95; m/z 230 (M^++1, <1%), 201 (32), 200 (100), 186 (12), 167 (18), 143 (15), 115 (15); HRMS: M^+, found 229.1461. $C_{15}H_{19}NO$ requires 229.1467.

2,2-Dimethyl-1-pyrazylpropanol (11a).[41] Pale yellow oil, t_r 9.7; R_f 0.63 (ethyl acetate); ν (film) 3400 (OH), 3052, (HC=C), 1071, 1017 cm^{-1} (CO); δ_H ($CDCl_3$) 0.94 (9H, s, 3×CH_3), 3.71, 4.46 (1 and 1H, respectively, 2s, CHOH), 8.50–8.55, (3H, m, ArH); δ_C ($CDCl_3$) 25.7 (3C), 36.4, 78.95, 142.85, 143.3, 144.4, 155.9; m/z 151 (M^+−CH_3, <1%), 110 (100), 57 (38), 41 (38).

1-Phenyl-1-pyrazylmethanol (11b).[42] Pale yellow oil, t_r 13.1; R_f 0.54 (ethyl acetate); ν (film) 3330 (OH), 3060, 1666 (HC=C), 1062 cm^{-1} (CO); δ_H ($CDCl_3$) 4.82 (1H, s, OH), 5.85 (1H, s, CHO), 7.25–7.40, 8.38, 8.43, 8.60 (5, 1, 1and 1H, respectively, s, 3d, respectively, J=2.4, 2.4, and 1.2 Hz, respectively, ArH); δ_C ($CDCl_3$) 74.25, 126.7 (2C), 128.0, 128.6 (2C), 141.8, 142.85, 143.0, 143.1, 157.25; m/z 187 (M^++1, 7%), 186 (M^+, 55), 185 (12), 184 (17), 170 (10), 169 (31), 168 (11), 156 (14), 107 (29), 105 (78), 91 (13), 81 (42), 80 (76), 79 (66), 78 (17), 77 (100), 53 (34), 52 (36), 51 (55), 50 (21), 44 (40), 43 (24).

3-Pyrazylpentan-3-ol (11c). Pale yellow oil, t_r 8.8; R_f 0.73 (ethyl acetate); ν (film) 3366 (OH), 1660, (HC=C), 1141 cm^{-1} (CO); δ_H ($CDCl_3$) 0.72 (6H, t, J=7.3 Hz, 2×CH_3), 1.85–1.95 (4H, m, 2×CH_2), 4.26 (1H, s, OH), 8.45–8.70 (3H, m, ArH); δ_C ($CDCl_3$) 7.6 (2C), 34.3 (2C), 76.15, 142.15, 142.45, 142.65, 159.25; m/z 166 (M^+, <1%), 138 (18), 137 (100), 119 (32), 94 (11), 92 (10), 81 (22), 80 (15), 57 (13), 54 (10), 53 (21), 52 (19), 45 (16); HRMS: M^+, found 166.1098. $C_9H_{14}N_2O$ requires 166.1106.

1-Phenyl-1-pyrazylethanol (11d). Pale yellow oil, t_r 13.4; R_f 0.70 (ethyl acetate); ν (film) 3360 (OH), 3082, 3057, 1667 (HC=C), 1090 cm^{-1} (CO); δ_H ($CDCl_3$) 1.99 (3H, s, CH_3), 7.25–8.50, 8.71 (8 and 1H, respectively, m and d, respectively, J=1.2 Hz, OH and ArH); δ_C ($CDCl_3$) 29.1, 74.85, 125.7 (2C),127.4, 128.45 (2C), 142.3, 142.7, 142.9 (2C) 160.4; m/z 201 (M^++1, 2%), 200 (M^+, 13), 121 (16), 105 (20), 80 (12), 79 (12), 77 (13), 52 (10), 51 (12), 43 (100); HRMS: M^+, found 200.0943. $C_{12}H_{12}N_2O$ requires 200.0950.

2,2-Dimethyl-1-(3,6-dimethylpyrazyl)propanol (11e). Pale yellow oil, t_r 10.9; R_f 0.38 (hexane/ethyl acetate: 1:1); ν (film) 3462 (OH), 3044, 1573 (HC=C), 1054 cm^{-1} (CO); δ_H ($CDCl_3$) 0.93 (9H, s, 3×CH_3CCO), 2.51 (3H, s, CH_3C=C), 2.55 (3H, s, CH_3C=CH), 3.87, 4.59 (1 and 1H, respectively, 2d, J=9.8 Hz, CHOH), 8.26 (1H, s, HCN); δ_C ($CDCl_3$) 20.8, 21.35, 25.8 (3C), 37.8, 75.65, 141.9, 148.05, 149.05, 152.85; *m/z* 194 (M^+, <1%), 138 (66), 137 (100), 122 (10), 120 (10), 107 (31), 57 (23), 42 (34), 41 (38), 40 (11); HRMS: M^+, found 194.1415. $C_{11}H_{18}N_2O$ requires 194.1419.

1-Phenyl-1-(3,6-dimethylpyrazyl)methanol (11f).[43] Pale yellow oil, t_r 14.2; R_f 0.36 (hexane/ethyl acetate: 1:1); ν (film) 3384 (OH), 3060, 3029, 1602 (HC=C), 1046 cm^{-1} (CO); δ_H ($CDCl_3$) 2.27 (3H, s, CH_3CC), 2.52 (3H, s, C*H*$_3$CCH), 5.72 (1H, s, OH), 5.76 (1H, s, CHO), 7.24, 8.22 (5 and 1H, respectively, 2s, ArH); δ_C ($CDCl_3$) 20.15, 20.4, 72.0, 127.1 (2C), 127.45, 128.1 (2C), 141.0, 141.75, 147.9, 148.55, 152.15; *m/z* 215 (M^++1, 16%), 214 (M^+, 100), 195 (12), 137 (24), 109 (28), 108 (82), 107 (67), 91 (22), 81 (11), 80 (16), 79 (38), 77 (45), 52 (11), 51 (25), 42 (62), 41 (13), 40 (14).

1-(3,6-Dimethylpyrazyl)cyclohexanol (11g). Pale yellow oil, t_r 13.2; R_f 0.59 (hexane/ethyl acetate: 1:1); ν (film) 3382 (OH), 3036, 1569 (HC=C), 1119 cm^{-1} (CO); δ_H ($CDCl_3$) 1.25–2.15 (10H, m, 5×CH_2), 2.51 (3H, s, CH_3CC), 2.75 (3H, s, C*H*$_3$CCH), 5.49 (1H, s, OH), 8.26 (1H, s, HCN); δ_C ($CDCl_3$) 20.5, 23.65, 21.75, 25.2 (2C), 35.4 (2C), 72.6, 141.1, 147.5, 147.7, 156.55; *m/z* 207 (M^++1, 4%), 206 (M^+, 27), 188 (15), 187 (19), 178 (40), 177 (11), 173 (14), 164 (19), 163 (89), 159 (17), 151 (38), 149 (15), 146 (11), 145 (12), 136 (22), 135 (92), 133 (14), 122 (82), 109 (57), 108 (76), 107 (75), 81 (24), 67 (11), 66 (13), 55 (29), 54 (15), 53 (19), 43 (32), 42 (100), 41 (49), 40 (28); HRMS: M^+, found 206.1416. $C_{12}H_{18}N_2O$ requires 206.1419.

1-(3,6-Dimethylpyrazyl)-1-phenylethanol (11h). White solid, mp 105–106°C (ethyl acetate/hexane); [Found: C, 73.39; H, 7.06; N, 11.89. $C_{14}H_{16}N_2O$ requires C, 73.66, H, 7.06, N, 12.27%]; t_r 14.4; R_f 0.55 (hexane/ethyl acetate: 1:1); ν (film) 3349 (OH), 3059, 3027, 1573 (HC=C), 1175 cm^{-1} (CO); δ_H ($CDCl_3$) 1.93 (3H, s, CH_3CO), 2.10 (3H, s, CH_3CC), 2.58 (3H, s, C*H*$_3$CCH), 6.29 (1H, d, *J*=2.4 Hz, OH), 7.28, 8.29 (5 and 1H, respectively, 2s, ArH); δ_C ($CDCl_3$) 20.65, 22.3, 26.4, 74.0, 126.25 (2C), 127.25, 128.1 (2C), 142.0, 144.65, 147.5, 148.7, 155.8; *m/z* 229 (M^++1, 5%), 228 (M^+, 37), 151 (11), 121 (18), 109 (16), 108 (100), 107 (36), 77 (16), 51 (10), 43 (89), 42 (39).

***N*-Phenyl-*N*-[1-phenyl-(3,6-dimethylpyrazyl)]methylamine (11i).** Yellow oil, t_r 18.3; R_f 0.71 (hexane/ethyl acetate:1:1); ν (film) 3386 (NH), 3048, 3026, 1602 cm^{-1} (HC=C); δ_H ($CDCl_3$) 2.56, 2.58 (3 and 3H, respectively, 2s, 2×CH_3), 5.73 (1H, s, C*H*NH), 6.65–6.70, 7.10–7.45, 8.22 (3, 8 and 1H, respectively, 3m and s, respectively, NH and ArH); δ_C ($CDCl_3$) 21.15 (2C), 58.2, 113.7, 117.55 (2C), 127.5, 127.85 (2C), 128.55 (2C), 129.15 (2C), 140.55, 141.9, 146.55, 147.8, 150.25, 152.5; *m/z* 290 (M^++1, 4%), 289 (M^+, 21), 197 (42), 183 (14), 182 (100), 104 (13), 77 (37), 51 (13), 42 (17); HRMS: M^+, found 289.1583. $C_{19}H_{19}N_3$ requires 289.1579.

3,6-Dimetylpyrazyl phenyl ketone (11j). Pale yellow oil, t_r 14.2; R_f 0.59 (hexane/ethyl acetate: 1:1); ν (film) 3055, 1596 (HC=C), 1673 cm^{-1} (C=O); δ_H ($CDCl_3$) 2.57 (6H, s, 2×CH_3), 7.45–7.90, 8.49 (5 and 1H, respectively, m and s, respectively, ArH); δ_C ($CDCl_3$) 21.0, 21.2, 128.55 (2C), 130.5 (2C), 133.8, 141.85, 144.55 (2C), 149.25, 149.7, 194.25; *m/z* 213 (M^++1, 6%), 212 (M^+, 40), 211 (28), 183 (25), 105 (100), 77 (68), 51 (24), 42 (30); HRMS: M^+, found 212.0946. $C_{13}H_{12}N_2O$ requires 212.0950.

2,2-Dimethyl-1-(2,6-dimethoxypyrimidin-4-yl)propan-1-ol (14a). Pale yellow oil, t_r 12.7; R_f 0.79 (hexane/ethyl acetate: 1:1); ν (film) 3441 (OH), 1598 (HC=C), 1104 cm^{-1} (CO); δ_H ($CDCl_3$) 0.93 (9H, s, 3×CH_3C), 3.83, 4.17 (1 and 1H, respectively, 2d, *J*=7.3 Hz, CHOH), 3.97, 3.98 (3 and 3H, respectively, 2s, 2×CH_3O), 6.28 (1H, s, HC=C); δ_C ($CDCl_3$) 25.7 (3C), 35.8, 53.7, 54.5 (2C), 79.85, 99.95, 164.3, 170.7, 171.2; *m/z* 227 (M^++1, <1%), 170 (48), 169 (100), 155 (21), 72(15), 57 (16), 42 (10), 41 (23); HRMS: M^+, found 226.1310. $C_{11}H_{18}N_2O_3$ requires 226.1317.

(2,6-Dimethoxypyrimidin-4-yl)-1-phenylmethanol (14b). White solid, mp 122–124°C (ethyl acetate/hexane); [Found: C, 63.53; H, 5.63; N, 11.02. $C_{13}H_{14}N_2O_3$ requires C, 63.40, H, 5.73, N, 11.38%]; t_r 15.9; R_f 0.42 (hexane/ethyl acetate: 1:1); ν (KBr) 3234 (OH), 3106, 1592 (HC=C), 1050 cm^{-1} (CO); δ_H ($CDCl_3$) 3.91, 3.98 (3 and 3H, respectively, 2s, 2×CH_3O), 4.50 (1H, s, OH), 5.55 (1H, s, CHO), 6.25, 7.25–7.40 (1 and 5H, respectively, s and m, respectively, ArH); δ_C ($CDCl_3$) 53.85, 54.7 (2C), 74.55, 97.95, 126.7 (2C), 127.9, 128.4 (2C), 141.65, 164.7, 172.0 (2C); *m/z* 247 (M^++1, 13%), 246 (M^+, 85), 245 (39), 229 (11), 169 (100), 141(17), 140 (60), 139 (11), 125 (41), 105 (12), 82 (18), 79 (26), 77 (48), 72 (19), 51 (21).

3-(2,6-Dimethoxypyrimidin-4-yl)pentan-3-ol (14c). White solid, mp 55–57°C (ethyl acetate/hexane); [Found: C, 58.71; H, 8.05; N, 11.79.$C_{11}H_{18}N_2O_3$ requires C, 58.39, H, 8.02, N, 12.38%]; t_r 12.7; R_f 0.63 (hexane/ethyl acetate: 1:1); ν (film) 3450 (OH), 1594 (HC=C), 1205 cm^{-1} (CO); δ_H ($CDCl_3$) 0.75 (6H, t, *J*=7.3 Hz, 2×C*H*$_3$CH$_2$), 1.70–1.90 (4H, m, 2×CH_2), 3.98, 4.02, (3 and 3H, respectively, 2s, 2×CH_3O), 4.15 (1H, s, OH), 6.34 (1H, s, HC=C); δ_C ($CDCl_3$) 7.55 (2C), 34.00 (2C), 53.9, 54.7 (2C), 76.6, 96.9, 164.35, 172.25, 175.0; *m/z* 227 (M^++1, <1%), 198 (28), 197 (100), 183 (15), 72 (21).

2-(2,6-Dimethoxypyrimidin-4-yl)-3-methylbutan-2-ol (14d). Pale yellow oil, t_r 12.6; R_f 0.70 (ethyl acetate); ν (film) 3441 (OH), 1596 (HC=C), 1207 cm^{-1} (CO); δ_H ($CDCl_3$) 0.75, 0.96 [3 and 3H, respectively, 2d, *J*=7.3 Hz, (C*H*$_3$)$_2$CH], 1.42 (3H, s, CH_3CO), 1.90–2.05 [1H, hept., C*H*(CH$_3$)$_2$], 3.98, 4.01, (3 and 3H, 2s, 2×CH_3O), 4.05 (1H, s, OH), 6.36 (1H, s, HC=C); δ_C ($CDCl_3$) 16.75, 17.05 (2C), 25.3, 37.85, 53.95, 54.75 (2C), 75.85, 96.9, 164.3, 172.2, 176.45; *m/z* 227 (M^++1, <1%), 184 (22), 183 (100), 151 (12), 72(25), 43 (31), 42 (10), 41 (13); HRMS: M^+, found 226.1327. $C_{11}H_{18}N_2O_3$ requires 226.1317.

2-(4,6-Dimethoxy-1,3,5-triazin-2-yl)propan-2-ol (14e). Pale yellow oil, t_r 10.9; R_f 0.52 (hexane/ethyl acetate: 1:1); ν (film) 3417 (OH), 1023 cm^{-1} (CO); δ_H ($CDCl_3$) 1.55 [6H, s, (C*H*$_3$)$_2$C], 1.60 (1H, s, OH), 4.08, (6H, s, 2CH_3O); δ_C ($CDCl_3$) 28.9 (2C), 55.4 (2C), 72.9, 172.5, 186.95; *m/z* 184 (M^+−CH_3, 100%), 141 (31), 126 (24), 72 (51), 70 (33), 69 (17), 59 (20), 58 (36), 43 (49), 42 (58), 41

(12); HRMS: M^+-CH_3, found 184.0725. $C_7H_{10}N_3O_3$ requires 184.0722.

3-(4,6-Dimethoxy-1,3,5-triazin-2-yl)pentan-3-ol (14f). Pale yellow oil, t_r 12.4; R_f 0.74 (hexane/ethyl acetate: 1:1); ν (film) 3472 (OH), 1108, 1066 cm^{-1} (CO); δ_H ($CDCl_3$) 0.75 (6H, t, J=7.6 Hz, 2×CH_3CH_2), 1.75–2.00 (4H, m, 2×CH_2), 3.77 (1H, s, OH), 4.08, (6H, s, 2×CH_3O); δ_C ($CDCl_3$) 7.4 (2C), 33.00 (2C), 55.05 (2C), 77.75, 172.0 (2C), 185.45; m/z 228 (M^++1, <1%), 199 (14), 198 (100), 72 (39), 70 (12), 58 (26), 57 (15), 42 (30); HRMS: M^+, found 227.1285. $C_{10}H_{17}N_3O_3$ requires 227.1270.

Preparation of 1-phenyl-1-(pyrid-2-yl)pentylamine (2′k).

To a green suspension of lithium powder (100 mg, 14.4 mmol) and naphthalene (40 mg, 0.31 mmol) in THF (15 mL) was slowly added (ca 10 min) a solution of 2-chloropyridine (**1a**, 4 mmol) and benzonitrile (5 mmol) in THF (5 mL) at −78°C under an argon atmosphere. Stirring was continued for 2 h at the same temperature. To the resulting mixture was then added toluene (30 mL), titanium tetraisopropoxide (2.4 mL, 8.0 mmol) and butylmagnesium chloride (10 mL, 20 mmol). The resulting mixture is allowed to rise to room temperature overnight and then is hydrolysed with NaOH (3 M, 5 mL). The mixture was filtered through celite, and the solution was extracted with ethyl acetate (2×40 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvents were evaporated (15 Torr) to give a residue, which was purified by column chromatography (silica gel, hexane/ethyl acetate), affording the pure title compound **2′k**. Yield is included in the text. Physical, spectroscopic and analytical data follow: yellow oil, t_r 15.0; R_f 0.31 (hexane/ethyl acetate: 1:1); ν (film) 3329 (NH), 3059, 3025, 1587 cm^{-1} (HC=C); δ_H ($CDCl_3$) 0.88 (3H, t, J=7.0 Hz, CH_3), 1.25–1.55 [4H, m, $CH_3(CH_2)_2$], 2.19 (2H, s, NH_2), 2.57 (2H, t, J=7.3 Hz, CH_2CN), 7.05–7.60, 8.50–8.55 (8 and 1H, respectively, 2m, ArH); δ_C ($CDCl_3$) 13.95, 20.45, 32.35, 47.75, 68.6, 121.75, 121.8, 127.15, 127.6 (2C), 128.45 (2C), 136.45, 142.86, 149.05, 162.8; m/z 241 (M^++1, <1%), 170 (16), 169 (100), 168 (71), 167 (31), 162 (16), 106 (10), 83 (14); HRMS: M^+, found 240.1641. $C_{16}H_{20}N_2$ requires 240.1626.

Demethylation of pyrimidines 14

*Isolation of 6-substituted uracils **16**. General procedure*—a mixture of the corresponding pyrimidine **14** (0.3 mmol) in 45% hydrobromic acid (3 mL) and glacial acetic acid (3 mL) is refluxed during 3 h and then, the resulting solution is quenched by addition of water (5 mL). The resulting mixture was extracted with ethyl acetate (4×15 mL). The organic layer was washed with brine (2×10 mL) and dried over anhydrous Na_2SO_4. The solvents were evaporated (15 Torr) to give a residue which was dissolved in methanol. To this new solution were added a few drops of ethyl acetate and hexane, recrystallizing the pure title compound. Yields are included in Table 5. Physical, spectroscopic and analytical data follow:

6-(2,2-Dimethyl-1-hydroxypropyl)uracil (16a). White solid, mp 243–245°C decompose; [Found: C, 51.53; H, 6.93; N, 12.45. $C_9H_{14}N_2O_3\cdot 3/4H_2O$ requires C, 51.05, H, 7.38, N, 13.23%]; R_f 0.44 (ethyl acetate); ν (film) 3368, 3232 (OH, NH), 1693 (C=O), 1628 (C=C), 1087 cm^{-1} (CO); δ_H (CD_3OD) 0.93 [9H, s, $(CH_3)_3C$], 4.0, (1H, s, CHO), 5.49 (1H, s, HC=C); δ_C (CD_3OD) 26.5 (3C), 36.5, 78.2, 99.6, 153.1, 159.7, 167.05; m/z (DIP) 199 (M^++1, 1%), 198 (M^+, 4), 142 (80), 71 (16), 70 (17), 68 (26), 57 (100), 44 (10), 43 (19), 42 (22), 41 (67).

6-(1-Ethyl-1-hydroxypropyl)uracil (16b). White solid, mp >330°C; [Found: C, 54.58; H, 7.15; N, 14.08. $C_9H_{14}N_2O_3$ requires C, 54.53, H, 7.12, N, 14.13%]; R_f 0.44 (ethyl acetate); ν (film) 3393 (OH, NH), 1708 (C=O), 1666 (HC=C), 1173 cm^{-1} (CO); δ_H (CD_3SOCD_3) 0.71 (6H, t, J=7.3 Hz, 2×CH_3), 1.45–1.60, 1.70–1.80 (2 and 2H, respectively, 2m, 2×CH_2), 4.97, (1H, s, OH), 5.48 (1H, s, HC=C), 10.16, 10.92 (1 and 1H, respectively, 2×NH); δ_C (CD_3SOCD_3) 7.4 (2C), 31.5 (2C), 74.55, 97.5, 151.65, 159.75, 164.0; m/z (DIP) 199 (M^++1, 1%), 198 (M^+, 5), 170 (48), 169 (15), 126 (100), 84 (10), 70 (17), 68 (37), 57 (66), 55 (13), 45 (15), 44 (12), 43 (28), 42 (15), 41 (27).

6-(1,2-Dimethyl-1-hydroxypropyl)uracil (16c). White solid, mp 201–203°C; [Found: C, 54.48; H, 7.09; N, 14.09. $C_9H_{14}N_2O_3$ requires C, 54.53, H, 7.12, N, 14.13%]; R_f 0.44 (ethyl acetate); ν (film) 3208 (OH, NH), 3041, 1660 (HC=C) 1712 (C=O), 1087 cm^{-1} (CO); δ_H (CD_3OD) 0.82, 0.92 [3 and 3H, respectively, 2d, J=4.4 Hz, $(CH_3)_2CH$], 1.37 (3H, s, CH_3CO), 1.85–1.90 [1H, m, $(CH_3)_2CH$], 5.55 (1H, d, J=3.7 Hz, HC=C); δ_C (CD_3OD) 16.7, 17.3 (2C), 25.0, 37.6, 75.35, 97.4, 153.15, 164.55, 167.4; m/z (DIP) 156 (M^+−42, 6%), 70 (8), 68 (8), 57 (6), 45 (8), 44 (11).

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