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ORIGINAL PAPER

Facile one-pot synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrroles using supported hydrogen sulfate ionic liquid

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Abstract Twelve new derivatives of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrrole were prepared by one-pot acid-catalyzed cyclocondensation reaction of 3-hydroxypyrrole, malononitrile, and various aldehydes in the presence of the silica-supported ionic liquid 1-methyl-3-(triethoxysilylpropyl)imidazolium hydrogen sulfate as catalyst. The reaction efficiencies were enhanced by moderate electron-withdrawing groups, such Cl and Br, on benzaldehyde, but decreased as substituents became more electron-withdrawing. Among the solvents and catalysts screened for the model reaction, acetonitrile and the silica-supported hydrogen sulfate ionic liquid were found to be the best choices.

Keywords Supported ionic liquids · Supported catalysts · One-pot synthesis · 5-Amino-7-aryl-6-cyano-4*H*-pyrano-[3,2-*b*]pyrrole · Hydrogen sulfate ionic liquid

Introduction

In recent years, ionic liquids have become a powerful alternative to conventional molecular organic solvents due to their particular properties, such as undetectable vapor pressure and the ability to dissolve many organic and inorganic substances [1]. In addition, ionic liquids are readily recycled and tunable to specific chemical tasks. One type is Brønsted acidic task-specific ionic liquids (BAILs). Among these, ionic liquids possessing HSO_4^- as a counteranion find a broad application in organic synthesis, acting as both solvents and catalysts. Recently, immobilization processes involving acidic ionic liquids on solid supports have been designed [2–8]. The heterogenization of catalysts and reagents can offer important advantages in handling, separation, and reuse procedures. On the basis of economic criteria, it is desirable to minimize the amount of ionic liquid utilized in a potential process. Immobilized acidic ionic liquids have been used as novel solid catalysts for a wide spectrum of reactions [9–13].

Homogeneous catalysts could be heterogenized through covalent and non-covalent attachment to either inorganic or organic materials, such as silica [14, 15], layered clay [16, 17], and polymers [18, 19]. Compared with organic supports, higher chemical and thermal stability are the most important advantages which are offered by inorganic supports. Despite having advantages, such as the increased flexibility in the choice of the support material, reaction conditions, and work-up strategies, non-covalent attachment enhances leaching of the catalyst from the support, leading to higher losses in activity of non-covalent catalysts in comparison with covalent analogues [20].

4*H*-Pyran derivatives are of interest in the area of synthesizing various drugs owing to their various pharmacological and biological activities, such as antimicrobial [21], mutagenicity [22, 23], antiproliferative [24], sex pheromone [25], antitumor [26], cancer therapy [27–29], and central nervous system activity [30]. Some of these compounds are widely employed as cosmetics and pigments and as potentially biodegradable agrochemicals [31]. Accordingly, the synthesis of such compounds is an interesting challenge.

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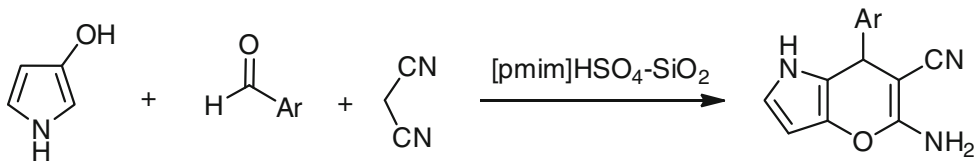
Scheme 1



With the aim of obtaining more biologically potent heterocyclic systems, many efforts have recently been undertaken for the preparation of various pyran derivatives, such as benzopyrans [32, 33], naphthopyrans [34–36], and 4-substituted pyrans [37], but to the best of our knowledge, the synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]-pyrrole derivatives has never been communicated until now. With these considerations in mind, we now report the synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]-pyrroles by one-pot cyclocondensation reaction of 3-hydroxypyrrole, substituted benzaldehydes, and malononitrile in the presence of 1-methyl-3-(triethoxysilylpropyl)-imidazolium hydrogen sulfate ([pmim]HSO_4–SiO_2) as a silica-supported ionic liquid with an acidic counteranion HSO_4^- (Scheme 1; Fig. 1).

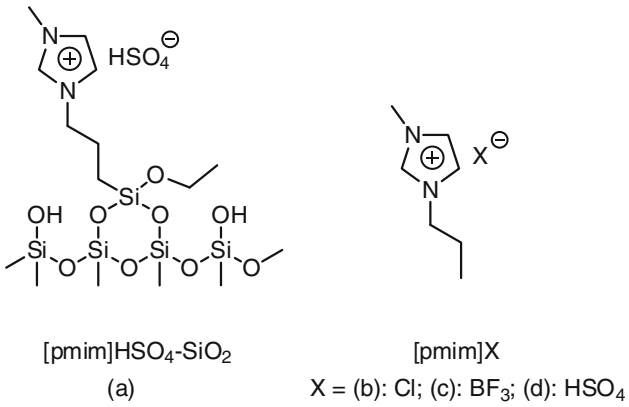


Fig. 1 Silica-supported ionic liquid catalyst (**a**), and unsupported ionic liquid catalysts (**b–d**)

Results and discussion

A mixture of benzaldehyde, 3-hydroxypyrrole, and malononitrile with a stoichiometric ratio of 1.0:1.0:1.1 and 10% mol of ionic liquid catalyst was chosen as the model reaction. To find the most efficient catalyst, three ionic liquids [pmim]HSO_4 (1-propyl-3-methylimidazolium–HSO_4), [pmim]BF_4 (1-propyl-3-methylimidazolium–BF_4), and [pmim]Cl (1-propyl-3-methylimidazolium–Cl), possessing different counteranions (Fig. 1), were comparatively used for catalyzing the model reaction (Table 1, entries 2–5). As can be seen in Table 1, among the ionic liquid catalysts employed, only [pmim]HSO_4 showed a desirable catalytic efficiency (entry 3).

Induced by the significant advantages offered by supported catalysts, such as the ease of separation from the reaction mixture, significant reduction in problems of waste disposal, and reuse applications by recycling, much effort has been devoted by many research groups to their preparation in the area of transition metal catalyst mediated organic reactions in recent decades [38–40]. Therefore, among the prepared catalysts, the most active one, [pmim]HSO_4, was supported on modified silica to obtain the immobilized catalyst [pmim]HSO_4–SiO_2 (Fig. 1). Immobilization on silica support slightly enhanced the activity of the corresponding catalyst and shortened the reaction time significantly (Table 1, entry 1). The higher activity of the immobilized catalyst [pmim]HSO_4–SiO_2 compared with its unsupported analogue could be attributed to the participation of SiO_2 in the catalytic process. In order to support this hypothesis, we used the silica support as catalyst under the same reaction conditions and showed that it improved the efficiency of the reactions compared with the non-catalytic system (Table 1, compare entries 1 and 6).

Table 1 Comparison of the catalytic efficiency of various ionic liquids

Entry	Catalyst	Time/h	Yield/%[a]
1	–	24	0
2	[pmim]HSO_4–SiO_2	3	89
3	[pmim]HSO_4	7	76
4	[pmim]BF_4	6	8
5	[pmim]Cl	24	3
6	Silica support	20	11

Reaction conditions: 1.0 equiv. of 3-hydroxypyrrole, 1.0 equiv. of benzaldehyde, 1.0 equiv. of malononitrile, 10% mol of catalyst, 4 cm^3 CH_3CN, 50 °C

[a] Isolated yields

Although the results in Table 2 show good yields for reused catalyst, there is an observable trend in the results that indicates deactivation of the catalyst with repeated use. One possible reason for this loss in activity might be due to the dissociation of the ionic liquid catalyst from the silica support surface.

To delineate the effect of solvent on the catalytic efficiency of [pmim]HSO_4–SiO_2, several solvents were examined for the model reaction (Table 3). As a result of

Table 2 Reusability of [pmim]HSO_4–SiO_2

Run	Time/h	Yield/%[a]
1	3	89
2	3	87
3	3	88
4	3	83

Reaction conditions: 1.0 equiv. of 3-hydroxypyrrole, 1.0 equiv. of benzaldehyde, 1.0 equiv. of malononitrile, 10% mol of [pmim]HSO_4–SiO_2, 4 cm^3 solvent, 50 °C

[a] Isolated yields

Table 3 Effect of solvents on the catalytic efficiency of [pmim]HSO_4–SiO_2

Entry	Solvent	Time/h	Yield/%[a]
1	Benzene	4	63
2	CH_3CN	3	89
3	MeOH	7	34
4	EtOH	6	36
5	Toluene	5	69

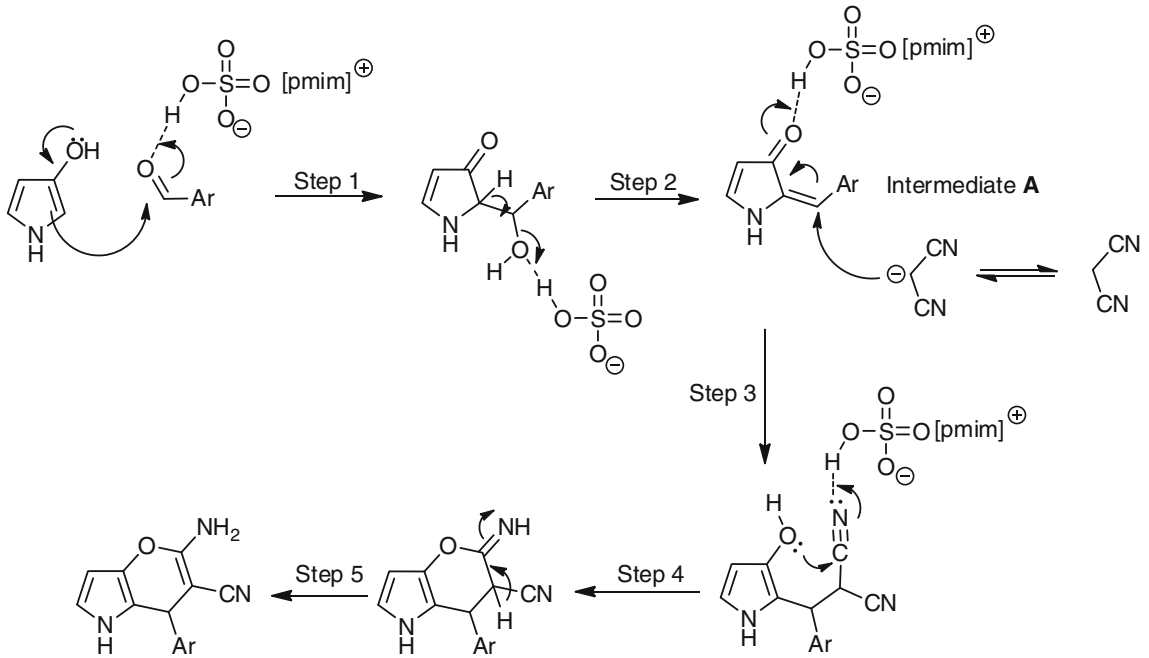
Reaction conditions: 1.0 equiv. of 3-hydroxypyrrole, 1.0 equiv. of benzaldehyde, 1.0 equiv. of malononitrile, 10% mol of [pmim]HSO_4–SiO_2, 4 cm^3 solvent, 50 °C

[a] Isolated yields

this investigation, protic solvents such as ethanol and methanol led to the worst results. Conversely, application of polar aprotic solvents such as acetonitrile significantly improved the chemical yields and reaction times. Compared with those obtained in protic solvents, chemical yields and reaction times were improved in apolar solvents, such as toluene and benzene, to some extent, but acetonitrile still remained the best solvent.

On the basis of recent reports which have proposed *ortho*-quinone methides (OQMs) as in situ intermediates in the one-pot three-component synthesis of naphthopyran derivatives [41, 42], we envisioned a mechanism with a similar intermediate (intermediate **A**) for the one-pot three-component synthesis of pyranopyrrole derivatives (Scheme 2). After Michael-type addition of malononitrile to intermediate **A**, the reaction is followed by attack of an hydroxyl group on one of two cyano groups to afford the final product.

To explore the scope of this reaction, we extended the model reaction using different derivatives of benzaldehyde. This revealed that the electronic nature of substituted groups on benzaldehyde could immensely affect the reaction times and chemical yields. Reaction efficiencies increased on changing the substituent groups from methoxy to Br and then Cl; however, the presence of more electron-withdrawing groups such as NO_2 and CN adversely affected the results (Table 4). This paradoxical behavior could be the result of a change in the rate-limiting step. In the case of electron-releasing or poorly electron-withdrawing groups, the first step, a nucleophilic attack of pyrrole on aldehyde, which is accelerated by electron-withdrawing groups, may be rate-limiting. On the other hand, the second step (dehydroxylation step) would probably become rate-limiting as the substituents become more electron-withdrawing. Because the second step proceeds



Scheme 2

Table 4 One-pot three-component synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrroles (Scheme 1)

Product	Ar	Time/h	Yield/%[a]
5a	4-CH_3O–C_6H_4	4	62
5b	C_6H_5	3	89
5c	4-CH_3–C_6H_4	3	80
5d	4-Br–C_6H_4	2	91
5e	2-Br–C_6H_4	2	89
5f	4-Cl–C_6H_4	1	88
5g	2-Cl–C_6H_4	1	88
5h	4-CN–C_6H_4	5	70
5i	2-CN–C_6H_4	5	67
5j	4-NO_2–C_6H_4	7	61
5k	2-NO_2–C_6H_4	8	69
5l	2-Furanyl	8	31

Reaction conditions: 1.0 equiv. of 3-hydroxypyrrole, 1.0 equiv. of aldehyde, 1.0 equiv. of malononitrile, 10% mol of [pmim]HSO_4–SiO_2, 4 cm^3 CH_3CN, 50 °C

[a] Isolated yields

better with electron-releasing groups, the presence of CN and NO_2 groups increases the reaction time and decreases the chemical yield.

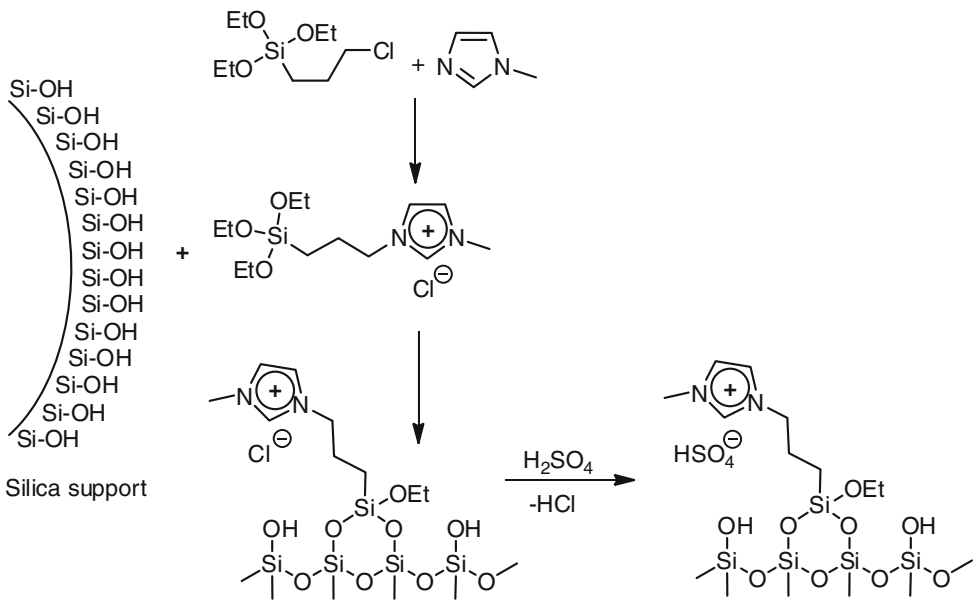
Experimental

All chemicals and accessible ionic liquids were purchased from Merck, Fluka, and Aldrich chemical companies. All yields refer to isolated products. The products were characterized by their spectral data. IR spectra were recorded on a Shimadzu-IR 470 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer in chloroform as the solvent and TMS as internal standard. Elemental analysis (C, H, N) was carried out by a PerkinElmer 2400 series-II elemental analyzer. The silica support, 1-methyl-3-(triethoxysilylpropyl)imidazolium chloride, [pmim]Cl–SiO_2, and [pmim]HSO_4–SiO_2 (extent of labeling 0.25 mmol/g loading) were prepared according to the literature (Scheme 3) [43].

Synthesis of silica support with extensive system of meso- and macropores

In a typical procedure 25 cm^3 1 M HNO_3 was dissolved in 2.3 g of polyethylene glycol (PEG) with molecular weight of 35,000 g/mol. The resultant sol was stirred until a clear solution was obtained. Then 22 cm^3 tetraethoxysilane (TEOS) was added slowly and after that 1 g of cetyltrimethylammonium bromide (CTAB). This solution was sonicated for 5 min, left to gel at 40 °C, and aged for 6 days at 40° C. Next the white alcogels obtained were impregnated in a 1 M NH_4OH solution for 10 h at 90 °C, washed with deionized water, dried for 4 days at 60 °C, and then calcined at 550 °C for 6 h under air (heating ramp 0.5 K/min). The size and shape of the monoliths were determined by the size and shape of the vessel used. Composition led to the formation of a macroporous, interconnected, open network with bimodal system of macropores of micrometer size. Apart from the macropores, the material also exhibited textural mesopores, with a BET surface area of 550 m^2/g, total pore volume 3.5 cm^3/g, and mean pore diameter of about 20 nm.

Scheme 3



Synthesis of 1-methyl-3-(triethoxysilylpropyl)-imidazolium chloride

A mixture of 0.12 mol (3-chloropropyl)triethoxysilane and 0.12 mol of 1-methylimidazole (freshly distilled) was refluxed at 78 °C for 24 h under nitrogen atmosphere. The reaction mixture was cooled and any remaining volatile substances were removed by rotary evaporation. The crude product was additionally washed with Et_2O (5×5 cm^3) and dried under vacuum. The product (slightly yellow viscous oil) was obtained in 98% yield.

Synthesis of 1-methyl-3-(triethoxysilylpropyl)-imidazolium chloride anchored on silica support ([pmim]Cl–SiO_2)

[Pmim]Cl (1 g, 2.7 mmol) was dissolved in 25 cm^3 of dry toluene and treated with 2 g of the previously prepared silica support. The slurry was heated at 90 °C for 16 h, after which the solid was isolated by filtration and washed with 100 cm^3 of dichloromethane. In the following step, the unreacted ionic liquid was removed by 24 h extraction with boiling dichloromethane. The material was then dried under high vacuum to give a white powder of [pmim]Cl–SiO_2 in 92% yield.

Synthesis of 1-methyl-3-(triethoxysilylpropyl)-imidazolium hydrogen sulfate anchored on silica support ([pmim]HSO_4–SiO_2)

In a three-necked round-bottom flask equipped with a stirrer, ice bath condenser, and thermometer, 3 g of [pmim]Cl–SiO_2 was suspended in 20 cm^3 of dry CH_2Cl_2. Under vigorous stirring 2.9 mmol of concentrated H_2SO_4 (97%) was added dropwise at 0 °C. The mixture was then warmed to room temperature and heated under reflux for 48 h. When the formed HCl was completely distilled off the solution was cooled and CH_2Cl_2 was removed under vacuum. To remove any water from the reaction mixture 10 cm^3 of benzene was added to the crude ionic liquid and stirred for 3 h with a magnetic stirrer at 50 °C. The formed azeotrope was distilled off yielding [pmim]HSO_4–SiO_2 in 93% yield.

*General procedure for synthesis of pyranopyrrole derivatives **5a–5l***

A mixture of aldehyde (1 mmol), 3-hydroxypyrrole (1 mmol), malononitrile (1.0 mmol) and ionic liquid catalyst (0.1 mmol) in 4 cm^3 CH_3CN was stirred at 50 °C for the appropriate time. The reaction was monitored by TLC and after completion of the reaction the catalyst was simply recovered by filtration and washed with dichloromethane. The residue was concentrated in vacuo and the crude product was purified by column chromatography on silica gel (Table 4).

5-Amino-1,7-dihydro-7-(4-methoxyphenyl)pyrano-[3,2-b]pyrrole-6-carbonitrile (**5a**, $C_{15}H_{13}N_3O_2$)
IR (KBr): $\bar{\nu}$ = 3,411 and 3,279 (asym. and sym. str. of $-NH_2$), 3,400 (NH), 2,160 ($-$CN str.), 1,251 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.37 (s, 3H, OCH_3), 5.43 (s, 1H, pyran H_4), 6.11 (d, 1H, pyrrole H_3), 6.63 (d, 2H, Ar–H), 6.68 (d, 1H, pyrrole H_2), 6.89 (s, 2H, D_2O exch., NH_2), 7.05 (d, 2H, Ar–H), 7.54 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.6 (pyran C_4), 55.2 (O–CH_3), 59.5 (pyran C_3), 101.5 (pyran C_6), 104.9 (pyrrole C_3), 119.3 (pyrrole C_1), 122.0 (CN), 126.1 (pyran C_5), 119.2, 127.4, 130.3, 154.6 (Ar–C), 171.4 (pyran C_2) ppm.

5-Amino-1,7-dihydro-7-phenylpyrano[3,2-b]-pyrrole-6-carbonitrile (**5b**, $C_{14}H_{11}N_3O$)
IR (KBr): $\bar{\nu}$ = 3,405 and 3,283 (asym. and sym. str. of $-NH_2$), 3,405 (NH), 2,157 ($-$CN str.), 1,247 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.51 (s, 1H, pyran H_4), 6.25 (d, 1H, pyrrole H_3), 6.73 (d, 1H, pyrrole H_2), 6.75 (s, 2H, D_2O exch., NH_2), 7.09–7.15 (m, 5H, Ar–H), 7.50 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.6 (pyran C_4), 55.8 (pyran C_3), 101.6 (pyran C_6), 106.4 (pyrrole C_3), 117.9 (pyrrole C_1), 123.5 (CN), 129.7 (pyran C_5), 122.8, 129.1, 127.9, 130.8 (Ar–C), 173.7 (pyran C_2) ppm.

5-Amino-1,7-dihydro-7-(4-methylphenyl)pyrano-[3,2-b]pyrrole-6-carbonitrile (**5c**, $C_{15}H_{13}N_3O$)
IR (KBr): $\bar{\nu}$ = 3,422 and 3,272 (asym. and sym. str. of $-NH_2$), 3,419 (NH), 2,189 ($-$CN str.), 1,252 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3H, Ar–CH_3), 5.60 (s, 1H, pyran H_4), 6.18 (d, 1H, pyrrole H_3), 6.80 (s, 2H, D_2O exch., NH_2), 6.89 (d, 1H, pyrrole H_2), 6.98–7.07 (m, 4H, Ar–H), 7.38 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.7 ($-CH_3$), 29.2 (pyran C_4), 54.6 (pyran C_3), 100.1 (pyran C_6), 107.3 (pyrrole C_3), 115.7 (pyrrole C_1), 126.5 (CN), 131.4 (pyran C_5), 128.3, 129.1, 133.6, 137.9 (Ar–C), 169.1 (pyran C_2) ppm.

5-Amino-7-(4-bromophenyl)-1,7-dihydropyrano[3,2-b]-pyrrole-6-carbonitrile (**5d**, $C_{14}H_{10}BrN_3O$)
IR (KBr): $\bar{\nu}$ = 3,425 and 3,269 (asym. and sym. str. of $-NH_2$), 3,434 (NH), 2,201 ($-$CN str.), 1,242 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.40 (s, 1H, pyran H_4), 6.11 (d, 1H, pyrrole H_3), 6.49 (s, 2H, D_2O exch., NH_2), 7.06 (d, 2H, Ar–H), 6.70 (d, 1H, pyrrole H_2), 7.25 (d, 2H, Ar–H), 7.39 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4 (pyran C_4), 64.9 (pyran C_3), 100.5 (pyran C_6), 109.5

(pyrrole C_3), 117.3 (pyrrole C_1), 127.2 (CN), 130.3 (pyran C_5), 123.6, 129.4, 130.9, 138.4 (Ar–C), 179.7 (pyran C_2) ppm.

5-Amino-7-(2-bromophenyl)-1,7-dihydropyrano[3,2-b]-pyrrole-6-carbonitrile (**5e**, $C_{14}H_{10}BrN_3O$)
IR (KBr): $\bar{\nu}$ = 3,415 and 3,298 (asym. and sym. str. of $-NH_2$), 3,411 (NH), 2,187 (−CN str.), 1,257 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.58 (s, 1H, pyran H_4), 6.19 (d, 1H, pyrrole H_3), 6.73 (d, 1H, pyrrole H_2), 6.79 (s, 2H, D_2O exch., NH_2), 6.97–7.11 (m, 4H, Ar–H), 7.58 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.3 (pyran C_4), 57.5 (pyran C_3), 108.6 (pyran C_6), 108.9 (pyrrole C_3), 121.6 (pyrrole C_1), 127.5 (CN), 131.5 (pyran C_5), 122.8, 122.4, 128.9, 132.7, 133.0, 141.6 (Ar–C), 179.0 (pyran C_2) ppm.

5-Amino-7-(4-chlorophenyl)-1,7-dihydropyrano-[3,2-b]pyrrole-6-carbonitrile (**5f**, $C_{14}H_{10}ClN_3O$)
IR (KBr): $\bar{\nu}$ = 3,414 and 3,259 (asym. and sym. str. of $-NH_2$), 3,415 (NH), 2,156 (−CN str.), 1,256 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.48 (s, 1H, pyran H_4), 6.16 (d, 1H, pyrrole H_3), 6.42 (s, 2H, D_2O exch., NH_2), 6.64 (d, 1H, pyrrole H_2), 7.06 (d, 2H, Ar–H), 7.21 (d, 2H, Ar–H), 7.29 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.7 (pyran C_4), 60.2 (pyran C_3), 106.5 (pyran C_6), 108.4 (pyrrole C_3), 119.0 (pyrrole C_1), 124.8 (CN), 136.1 (pyran C_5), 129.5, 129.4, 130.5, 132.8 (Ar–C), 179.7 (pyran C_2) ppm.

5-Amino-7-(2-chlorophenyl)-1,7-dihydropyrano-[3,2-b]pyrrole-6-carbonitrile (**5g**, $C_{14}H_{10}ClN_3O$)
IR (KBr): $\bar{\nu}$ = 3,458 and 3,256 (asym. and sym. str. of $-NH_2$), 3,397 (NH), 2,167 (−CN str.), 1,248 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.51 (s, 1H, pyran H_4), 6.28 (d, 1H, pyrrole H_3), 6.64 (d, 1H, pyrrole H_2), 6.84 (s, 2H, D_2O exch., NH_2), 7.09–7.19 (m, 4H, Ar–H), 7.43 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.2 (pyran C_4), 55.6 (pyran C_3), 113.9 (pyran C_6), 114.2 (pyrrole C_3), 118.6 (pyrrole C_1), 129.1 (CN), 137.2 (pyran C_5), 125.4, 127.3, 128.9, 132.7, 133.0, 139.6 (Ar–C), 173.7 (pyran C_2) ppm.

5-Amino-7-(4-cyanophenyl)-1,7-dihydropyrano-[3,2-b]pyrrole-6-carbonitrile (**5h**, $C_{15}H_{10}N_4O$)
IR (KBr): $\bar{\nu}$ = 3,401 and 3,248 (asym. and sym. str. of $-NH_2$), 3,418 (NH), 2,210 (−CN str.), 2,181 (−CN str.), 1,257 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.51 (s, 1H, pyran H_4), 6.10 (d, 1H, pyrrole H_3), 6.48 (s, 2H, D_2O exch., NH_2), 6.60 (d, 1H, pyrrole H_2), 7.24 (s, 1H, pyrrole NH), 7.26 (d, 2H, Ar–H), 7.38 (d, 2H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.6 (pyran C_4), 62.8 (pyran C_3), 111.7 (pyran C_6), 114.5 (pyrrole C_3), 122.4 (pyrrole C_1), 124.8 (CN), 126.5 (CN), 139.4 (pyran C_5), 114.8, 129.9, 133.5, 139.5 (Ar–C), 176.3 (pyran C_2) ppm.

5-Amino-7-(2-cyanophenyl)-1,7-dihydropyrano-[3,2-b]pyrrole-6-carbonitrile (**5i**, $C_{15}H_{10}N_4O$)
IR (KBr): $\bar{\nu}$ = 3,421 and 3,248 (asym. and sym. str. of $-NH_2$), 3,416 (NH), 2,201 (−CN str.), 2,190 (−CN str.), 1,250 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.59 (s, 1H, pyran H_4), 6.31 (d, 1H, pyrrole H_3), 6.60 (d, 1H, pyrrole H_2), 6.81 (s, 2H, D_2O exch., NH_2), 7.23–7.39 (m, 4H, Ar–H), 7.43 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.2 (pyran C_4), 59.6 (pyran C_3), 110.3 (pyran C_6), 110.9 (pyrrole C_3), 118.1 (pyrrole C_1), 120.3 (CN), 121.5 (CN), 134.2 (pyran C_5), 115.0, 128.2, 130.6, 132.5, 133.9, 141.3 (Ar–C), 174.8 (pyran C_2) ppm.

5-Amino-1,7-dihydro-7-(4-nitrophenyl)pyrano-[3,2-b]pyrrole-6-carbonitrile (**5j**, $C_{14}H_{10}N_4O_3$)
IR (KBr): $\bar{\nu}$ = 3,413 and 3,240 (asym. and sym. str. of $-NH_2$), 3,414 (NH), 2,178 (−CN str.), 1,360 and 1,548 (asym. and sym. str. of $-NO_2$), 1,249 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.50 (s, 1H, pyran H_4), 6.17 (d, 1H, pyrrole H_3), 6.40 (s, 2H, D_2O exch., NH_2), 6.57 (d, 1H, pyrrole H_2), 7.31 (s, 1H, pyrrole NH), 7.37 (d, 2H, Ar–H), 8.03 (d, 2H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4 (pyran C_4), 59.7 (pyran C_3), 107.8 (pyran C_6), 108.2 (pyrrole C_3), 120.5 (pyrrole C_1), 124.3 (CN), 136.8 (pyran C_5), 121.5, 129.1, 141.6, 145.3 (Ar–C), 177.4 (pyran C_2) ppm.

5-Amino-1,7-dihydro-7-(2-nitrophenyl)pyrano-[3,2-b]pyrrole-6-carbonitrile (**5k**, $C_{14}H_{10}N_4O_3$)
IR (KBr): $\bar{\nu}$ = 3,413 and 3,240 (asym. and sym. str. of $-NH_2$), 3,414 (NH), 2,178 (−CN str.), 1,381 and 1,547 (asym. and sym. str. of $-NO_2$), 1,253 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.51 (s, 1H, pyran H_4), 6.28 (d, 1H, pyrrole H_3), 6.57 (d, 1H, pyrrole H_2), 6.86 (s, 2H, D_2O exch., NH_2), 7.33–7.39 (m, 2H, Ar–H), 7.44 (s, 1H, pyrrole NH), 7.56 (dd, 1H, Ar–H), 8.01 (d, 1H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.0 (pyran C_4), 54.3 (pyran C_3), 110.9 (pyran C_6), 112.2 (pyrrole C_3), 121.2 (pyrrole C_1), 121.9 (CN), 137.7 (pyran C_5), 122.0, 128.4, 133.5, 134.9, 136.0, 148.8 (Ar–C), 177.0 (pyran C_2) ppm.

5-Amino-7-(2-furanyl)-1,7-dihydropyrano-[3,2-b]pyrrole-6-carbonitrile (**5l**, $C_{12}H_9N_3O_2$)
IR (KBr): $\bar{\nu}$ = 3,418 and 3,234 (asym. and sym. str. of $-NH_2$), 3,419 (NH), 2,166 (−CN str.), 1,252 (asym. str. of cyclic ArC–O–C ether) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.47 (s, 1H, pyran H_4), 5.87 (dd, 1H, furan H_3), 6.19 (m, 2H, pyrrole H_3, furan H_4), 6.59 (d, 1H,

pyrrole H_2), 6.78 (s, 2H, D_2O exch., NH_2), 7.24 (d, 1H, furan H_2), 7.40 (s, 1H, pyrrole NH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 29.4$ (pyran C_4), 56.4 (pyran C_3), 106.9 (pyran C_6), 107.0 (furan C_3), 110.3 (pyrrole C_3), 110.8 (furan C_4), 119.5 (pyrrole C_1), 116.4 (CN), 141.9 (furan C_2), 143.2 (pyran C_5), 150.9 (furan C_1), 167.4 (pyran C_2) ppm.

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