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Superacid-catalyzed reactions of pyridinecarboxaldehydes

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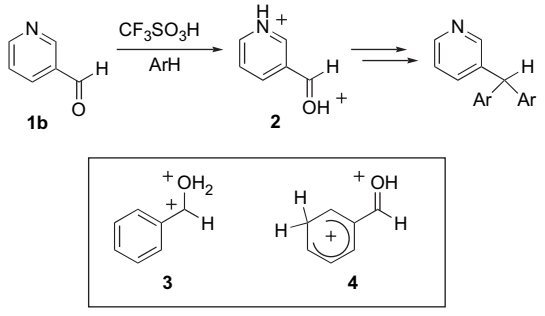
Abstract—A variety of pyridinecarboxaldehydes are shown to give condensation products in high yields (80–99%, 10 examples) by reacting with benzene and CF_3SO_3H (triflic acid). In the superacidic solution, pyridinecarboxaldehydes can react with deactivated arenes (*o*-dichlorobenzene and nitrobenzene) and with saturated hydrocarbons (methylcyclohexane and adamantane). Dicationic intermediates from pyridinecarboxaldehydes in superacid (FSO_3H–SbF_5) have been directly observed using low temperature ^{13}C NMR spectroscopy. Diprotonated pyridinecarboxaldehydes have also been studies using ab initio computational methods.

1. Introduction

We recently described the superacid-catalyzed chemistry of 3-pyridinecarboxaldehyde (**1b**), its reactions with deactivated arenes, and the involvement of dicationic electrophilic intermediates (Scheme 1).[1] Because of the similarities to the superelectrophilic systems like diprotonated benzaldehyde (**3**–**4**),[2] we proposed that dication **2** is a good model system for the superelectrophilic intermediates.[3] Since our report, many similar dicationic electrophilic systems have been described.[4] These reactive, dicationic electrophiles typically have a relatively stable cationic center (such as a pyridinium, ammonium, or phosphonium cation) adjacent to a cationic electrophilic site. We and others have shown that these dicationic electrophiles can exhibit dramatically increased electrophilic reactivities compared to analogous monocationic electrophiles.



Scheme 1.

In this paper, we provide a full report of our studies involving the superacid-catalyzed reactions of pyridinecarboxaldehydes (**1a**–**c**). The superacid-catalyzed condensation reactions of pyridinecarboxaldehydes with arenes are described and a general mechanism involving dicationic intermediates is proposed. These dicationic intermediates are also shown to be capable of reacting with saturated hydrocarbons. Direct observation of the dicationic species using low temperature NMR is also reported. The diprotonated species from 2-, 3-, and 4-pyridinecarboxaldehyde have also been studied using ab initio computational methods and these results are described. The results from these studies demonstrate that reactive dications can be formed in high concentrations and they exhibit electrophilic reactivities comparable to superelectrophiles.

2. Results and discussion

Some time ago, the condensations of pyridinecarboxaldehydes (**1a**–**c**) with benzene in H_2SO_4 were described in the patent literature.[5] Our previous report described the condensation of 3-pyridinecarboxaldehyde (**1b**) with benzene and CF_3SO_3H, and this Brønsted superacid was found to be an outstanding catalyst for the condensation.[1] In order to further demonstrate the utility of CF_3SO_3H in these types of condensation reactions, a series of pyridinecarboxaldehydes have been reacted with benzene in CF_3SO_3H (Table 1). The isomeric pyridinecarboxaldehydes (**1a**–**c**), and a number of substituted derivatives (**6**–**12**), give the condensation products in excellent yields. An *N*-methylated pyridiniumcarboxaldehyde also gives the condensation product (**21**) in high yield (Scheme 2). Although the yields have not been optimized, it has been determined that as little as 2.7 equiv of CF_3SO_3H can be used to convert **1a** to product **13a**

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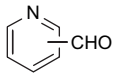
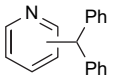
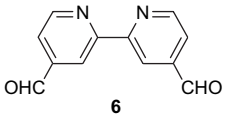
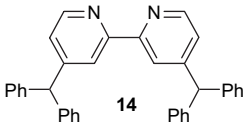
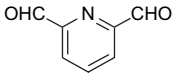
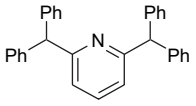
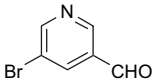
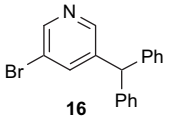
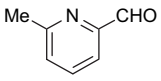
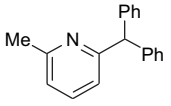
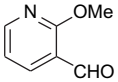
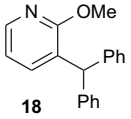
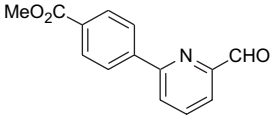
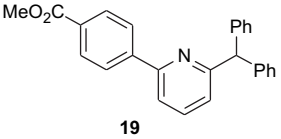
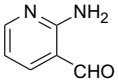
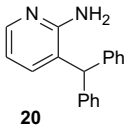
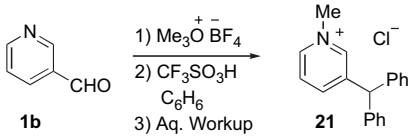
Table 1. Products and yields for the reactions of pyridinecarboxaldehydes (**1a–c**, **6–12**) with C_6H_6 and CF_3SO_3H

Starting material	Product	Yield (%)
		
1a, 2-isomer **1b**, 3-isomer **1c**, 4-isomer	**13a**, 2-isomer **13b**, 3-isomer **13c**, 4-isomer	88 99 93
 **6**	 **14**	80
 **7**	 **15**	82
 **8**	 **16**	92
 **9**	 **17**	90
 **10**	 **18**	99
 **11**	 **19**	89
 **12**	 **20**	91

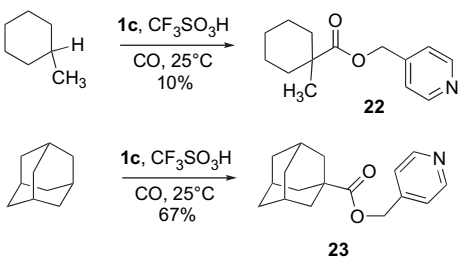
(>80% yield), and with larger quantities of CF_3SO_3H (15 equiv), the condensation reaction is complete within 5 min.[6] The condensation of **1a–13a** can be accomplished with H_2SO_4,[5] H_3PO_4,[5] and also $AlCl_3$,[7] but these acids give the hydroxy alkylation products (**13a–c**) in somewhat low yields (accompanied by unreacted **1a**). Recently, it was discovered that products **13a–c** are highly potent dopamine transporter inhibitors and it was proposed that these types of compounds may have therapeutic value in the treatment of cocaine abuse.[8] The triflic acid catalyzed reactions of pyridinecarboxaldehydes with benzene are effective, general route to these products.



Scheme 2.

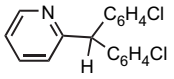
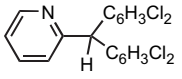
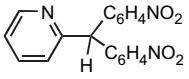
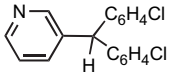
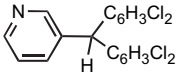
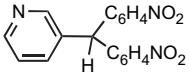
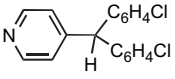
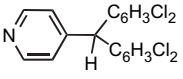
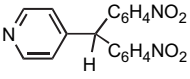
With less nucleophilic arenes, the pyridinecarboxaldehydes (**1a–c**) give hydroxy alkylation products from superacid (Table 2). The isomeric pyridinecarboxaldehydes were reacted with the deactivated arenes, chlorobenzene, *o*-dichlorobenzene, and nitrobenzene, in excess of CF_3SO_3H (100 equiv), and in all cases the condensation products were obtained. Remarkably, the pyridinecarboxaldehydes even react with nitrobenzene in a solution wherein the nitro group is largely protonated (protonated nitrobenzene, $pK_a=-11$).[9] Under similar conditions, benzaldehyde reacts with chlorobenzene in superacid to give some condensation product, but it does not react with either *o*-dichlorobenzene or nitrobenzene. Besides weak nucleophilic arenes, 4-pyridinecarboxaldehyde (**1c**) is also found to react with saturated hydrocarbons in superacid. When 4-pyridinecarboxaldehyde is dissolved in 6 equiv of CF_3SO_3H with 1.0 equiv of methylcyclohexane under CO pressure (750 psi; 25 °C), the functionalized product (**22**) is formed, al beit in low isolated yield (Scheme 3). Similarly, adamantane gives the ester product (**23**) in reasonable yield, along with a smaller amount of 1-adamantanecarboxylic acid. To verify that functionalization of the hydrocarbon is due to the reactivity of the carboxonium ion, methylcyclohexane was reacted with 6 equiv of CF_3SO_3H, CO (5 atm), and 4-pyridinemethanol. Under these conditions, there is no product (**22**) formed.

In order to characterize the electrophilic species arising from the pyridinecarboxaldehydes (**1a–c**), ab initio theoretical calculations were done along with spectroscopic studies. For the isomeric pyridinecarboxaldehydes (**1a–c**), 10 structures were located at potential energy minima on the energy surfaces for the *N*,*O*-diprotonated species (Fig. 1; all minimized structures possess C_1 symmetry). Geometry optimizations were done using density function theory and the hybrid functional B3LYP at the 6-311G** level.[10,11,12] Vibrational analyses were performed at the B3LYP/6-311G** level of theory and all optimized structures (**24–26**) were found to have zero imaginary frequencies. Zero-point-energy corrections were made to the single point energies for structures **24–26**. From 2-pyridinecarboxaldehyde (**1a**), four structures are found at energy minima: the conformational isomers of the *syn* stereoisomer (*syn*-**24a** and *syn*-**24b**) and *anti* stereoisomer (*anti*-**24a** and *anti*-**24b**) of the diprotonated



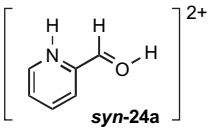
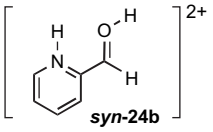
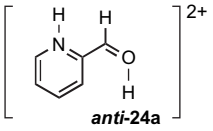
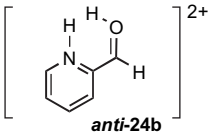
Scheme 3. Superacidic-functionalization of hydrocarbons with 4-pyridinecarboxaldehyde (**1c**).

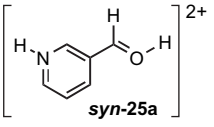
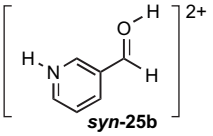
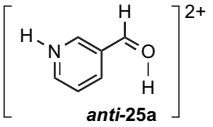
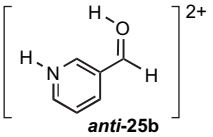
Table 2. Products and yields[a] from the reactions of pyridinecarboxaldehydes (**1a–c**) with deactivated arenes and CF_3SO_3H

Aldehyde	Chlorobenzene products[b]	Yield (%)	*o*-Dichlorobenzene products[c]	Yield (%)	Nitrobenzene products[d]	Yield (%)
1a		88		72		12
1b		85		87		10
1c		94		83		53

[a] Yields are reported as the mixture of isomers; result for **1b** is taken from Ref. 1.
[b] Reaction done at 25 °C.
[c] Reaction done at 80 °C.
[d] Reaction done at 140 °C.

aldehyde. The global energy minimum is found at the *syn*-**24b** structure, while the *syn*-**24a** structure is the next most stable structure, estimated to be 2.5 kcal/mol less stable than *syn*-**24b**. Diprotonation of 3-pyridinecarboxaldehyde (**1b**) also gives four structures at energy minima. The calculations find the global energy minimum at the *syn*-**25a**

structure	E + ZPE (Hartrees)	relative energy (kcal•mol^{-1})
 ***syn*-24a**	-362.095123	2.5
 ***syn*-24b**	-362.099126	0.0
 ***anti*-24a**	-362.083881	9.6
 ***anti*-24b**	-362.080414	11.7

structure	E + ZPE (Hartrees)	relative energy (kcal•mol^{-1})
 ***syn*-25a**	-362.109605	0.0
 ***syn*-25b**	-362.109488	0.1
 ***anti*-25a**	-362.098031	7.3
 ***anti*-25b**	-362.095243	9.0

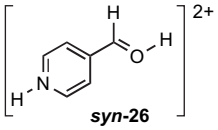
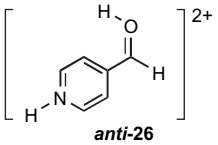
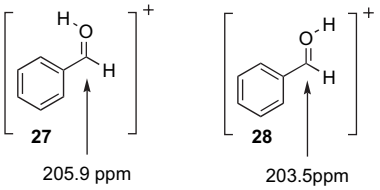
structure	E + ZPE (Hartrees)	relative energy (kcal•mol^{-1})
 ***syn*-26**	-362.105289	0.0
 ***anti*-26**	-362.093665	7.3

Figure 1. Calculated structures and energies for the diprotonated pyridinecarboxaldehydes (**24–26**) at the B3LYP/6-311G**//B3LYP/6-311G** level of theory.

structure, but the *syn*-**25b** structure is just 0.1 kcal/mol less stable. In the case of 4-pyridinecarboxaldehyde, the *syn*-**26** and *anti*-**26** structures (both C_1 point group) are found at energy minima, and the *syn*-**26** is more stable by 7.3 kcal/mol. These computational results are in accord with earlier studies related to protonated aldehydes. Experimental and theoretical results have previously shown that the *anti* stereoisomers of protonated aldehydes are less stable than the *syn* stereoisomers.[13] Interestingly, the monocationic carboxonium ions from benzaldehyde (**27**–**28**) are estimated to be 2.2 kcal/mol apart in relative energies for the *syn* and *anti* stereoisomers (Scheme 4).[2a] The dicationic carboxonium ions **24**–**26** show increasing relative energy differences for the *syn* and *anti* stereoisomers (7.3–11.7 kcal/mol).



Scheme 4.

The isomeric pyridinecarboxaldehydes were also studied by ^{13}C NMR in acidic solvents and the results are consistent with the formation of *N*,*O*-diprotonated structures in superacid (Table 3). When 2-pyridinecarboxaldehyde (**1a**) is dissolved in solutions of increasing acidity, the carbonyl (or carboxonium) carbon is progressively shifted down field from 181.9 ppm in CF_3CO_2H (H_o −2.7) to 203.6 ppm in SbF_5–FSO_3H (H_o<−18). The down field shifts indicate an increasing degree of protonation of the carbonyl group, and in SbF_5–FSO_3H, the chemical shift (203.6 ppm) is similar to other observed protonated aldehydes. For example, protonated benzaldehyde (**27** and **28**) gives carboxonium resonances at 203.5 and 205.9 ppm (Scheme 4).[2a] In our earlier communication, we described similar NMR experiments with 3-pyridinecarboxaldehyde (**1b**).[1] With increasing acidity, this compound also shows a dramatic down field shift of the carbonyl carbon. In the SbF_5–FSO_3H solution, however, two peaks are observed for the carbonyl carbon and several of the ring carbons. These doubled signals were initially thought to be from the *syn* and *anti* stereoisomers of the protonated aldehyde, because previous NMR studies of protonated aliphatic and aromatic aldehydes have observed both stereoisomers.[13] We now propose that the two observed ions are *not* the *syn* and *anti* stereoisomers, but rather the rotational isomers *syn*-**25a** and *syn*-**25b**. The computational studies indicated that these two rotational isomers are very close in energy, while the *syn* and *anti* isomers are energetically far apart. Evidently, a sizable energy barrier separates the conformational isomers *syn*-**25a** and *anti*-**25b**, because their inter-conversion is slow on the NMR time-scale at −80 °C.[13d] The NMR studies of 4-pyridinecarboxaldehyde (**1c**) also suggest the formation of the *N*,*O*-diprotonated species in superacid. The carbonyl ^{13}C resonance moves down field from 184.5 ppm in CF_3CO_2H to 211.2 ppm in SbF_5–FSO_3H solution. The ^{13}C NMR spectrum from SbF_5–FSO_3H solution clearly shows that a single species is generated from **1c** (Fig. 2). Computational results indicate that the *syn*-**26** structure would be heavily favored in an equilibration of diprotonated structures. Upon solvation in superacid, aldehyde **1c** is converted to the *syn*-**26** species, and at the highest levels of acidity (SbF_5–FSO_3H, H_o<−18) the conversion appears to be complete. The series of pyridinecarboxaldehydes (**1a**–**c**) give NMR spectra from superacid that are in accord with the results from the ab initio studies. For both **1a** and **1c**, calculations show that only one *N*,*O*-diprotonated species is located at or near the global minima, and the ^{13}C NMR spectra show only one species in each of the SbF_5–FSO_3H solutions. But calculations on the **1b** system show two species at or near the global minimum, and both ions are observed in the ^{13}C NMR.

Table 3. ^{13}C NMR data from pyridinecarboxaldehydes **1a**–**c** in acidic solution

Aldehyde	Acid system (H_o)	^{13}C NMR data, δ, ppm[a]
1a	CF_3CO_2H (−2.7)	181.9 (c), 148.4, 142.1, 140.0, 130.3, 128.4
	CF_3SO_3H (−14.1)	184.6 (c), 148.9, 142.1, 138.8, 131.1, 129.6
	FSO_3H (−15.1)	191.8 (c), 150.3, 144.4, 138.5, 133.7, 133.2
	SbF_5–FSO_3H (<−18)	203.6 (c), 150.6, 150.0, 145.3, 140.9, 133.0
1b	CF_3CO_2H	184.0 (c), 142.9, 140.2, 138.1, 129.2, 123.4
	CF_3SO_3H	193.3 (c), 147.1, 144.9, 142.3, 131.3, 127.5
	FSO_3H	201.0 (c), 149.7, 148.5, 146.1, 130.5, 129.5
	SbF_5–FSO_3H	208.6 (c), 155.8, 149.8, 144.6, 129.0, 125.2 207.1 (c), 151.4, 150.5, 148.6, 129.0, 125.2
1c	CF_3CO_2H	184.5 (c), 143.2, 138.3, 121.3
	CF_3SO_3H	194.6 (c), 142.1, 126.1, 122.8
	FSO_3H	199.6 (c), 143.9, 142.6, 127.0
	SbF_5–FSO_3H	211.2 (c), 143.3, 138.8, 130.4

(c) Indicates carbonyl (or carboxonium carbon) signal. Data for **1b** are taken from Ref. 1.

[a] Experiments with CF_3CO_2H or CF_3SO_3H were done at 25 °C; experiments with FSO_3H or SbF_5–FSO_3H were done at −70 °C with SO_2ClF diluent.

Based on the results of the NMR studies and the superacid-promoted reactions, a general mechanism is proposed that invokes these dicationic intermediates (Scheme 5). For example in the case of **1c**, the pyridine nitrogen is initially protonated to give the pyridinium cation (**29**) and subsequent protonation at the carbonyl oxygen yields the dicationic intermediate *syn*-**26**. Electrophilic attack of benzene then leads to the condensation products via dicationic intermediates **30** and **31**. In the case of 2-amino-3-pyridinecarboxaldehyde (**12**), the analogous tricationic electrophile (**33**) is likely generated from the dication **32**.[14] Given the low nucleophilicity of C_6H_6, it is highly unlikely that the condensation reaction occurs via the dication **32**, but must involve further protolytic activation of the carbonyl group. When 4-pyridinecarboxaldehyde (**1c**) is reacted with carbon monoxide and methylcyclohexane in CF_3SO_3H, the product is formed by hydride transfer from the cycloalkane to the dicationic carboxonium ion (Scheme 6). This proposed mechanism is in accord with another recent study showing the reduction of 3-pyridinecarboxaldehyde to 3-pyridilcarbinol and 3-methylpyridine from the reactions with

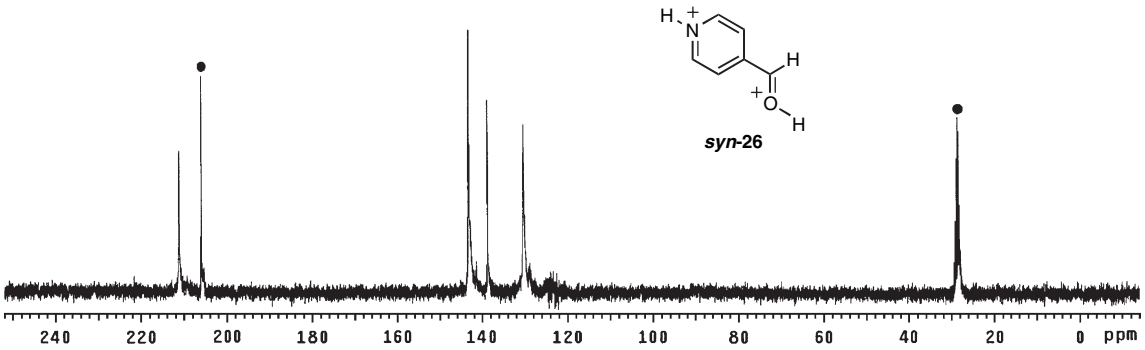
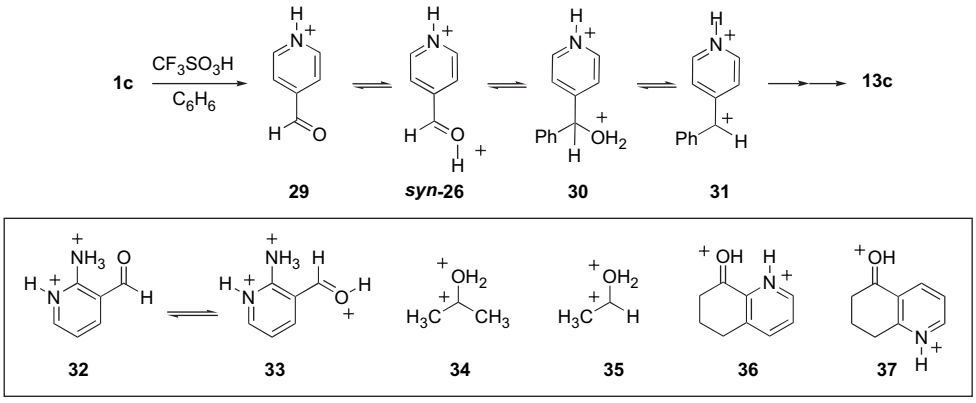
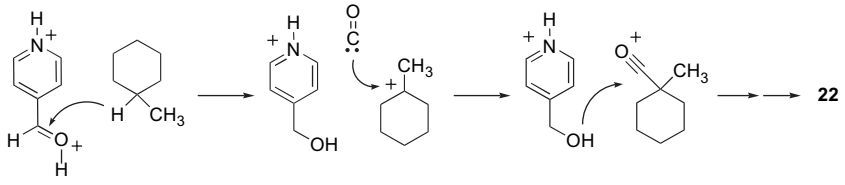


Figure 2. ^{13}C NMR spectrum of the dicationic product (*syn*-**26**) from 4-pyridinecarboxaldehyde (**1c**) and FSO_3H–SbF_5–SO_2ClF at −80 °C (• denotes external solvent, d_6-acetone).



Scheme 5. Proposed reaction mechanisms and intermediates in the electrophilic reactions of 4-pyridinecarboxaldehyde (**1c**) and related electrophiles.



Scheme 6.

cyclohexane and superacid or excess $AlCl_3$.[2c] In this recent study, the diprotonated species (**25**) is thought to be involved in hydride abstraction from cyclohexane. Because carboxonium ions are relatively weak electrophiles, there are few examples of carboxonium ions reacting with alkanes or cycloalkanes.[15] Superelectrophilic species like **34** and **35** are known to react with alkanes or cycloalkanes, while dicationic species like **36** and **37** have been shown to abstract hydride from cyclohexane–methylcyclopentane.[16]

In summary, a series of pyridinecarboxaldehydes are shown to give condensation products in excellent yields by reactions with arenes in the Brønsted superacid, CF_3SO_3H. The reactions involve dicationic intermediates, which exhibit very high electrophilic reactivities, attacking even *o*-dichlorobenzene, nitrobenzene, and some saturated hydrocarbons. Evidence for the involvement of dicationic intermediates comes from the direct observation of diprotonated species by low temperature ^{13}C NMR spectroscopy. For the diprotonated pyridinecarboxaldehydes, theoretical calculations show that the *syn*-carboxonium structures are strongly destabilized relative to the *anti*-forms, presumably due to the repulsive interaction of the cationic pyridinium ring and the carboxonium proton. These studies also show the importance of stable cationic groups in the structure–activity relationships of electrophilic systems. A high level of electrophilic reactivity can be achieved by the activation of the carboxonium group by the stable pyridinium cationic center.[17]

3. Experimental

3.1. General

The pyridinecarboxaldehydes were purchased from commercial suppliers and used as received. The trifluoromethanesulfonic acid (triflic acid) was purchased from the manufacturer and it was distilled from an Ar atmosphere prior to use. SbF_5 and triple distilled FSO_3H were purchased from commercial suppliers and used as received.

3.1.1. Procedure for the preparation of condensation products. The pyridinecarboxaldehyde (0.2 g, ca. 1 mmol) is dissolved in 1.0 mL of benzene, and 3 mL of CF_3SO_3H

is added. After 6 h, the mixture is poured over ice, the solution is neutralized with NaOH, and the products are extracted into $CHCl_3$. The organic extracts are then washed with H_2O, brine, and dried with $MgSO_4$. Concentration in vacuo provides the crude products, which are then purified by recrystallization or column chromatography.

3.1.2. Procedure for the reactions and functionalization of hydrocarbons. In a 125 mL Parr autoclave (glass-lined and flushed with dry Ar), 4-pyridinecarboxaldehyde (1 mmol) and methylcyclohexane (1 mmol) dissolved in 5 mL $CHCl_3$ and 3 mL CF_3SO_3H were added. The reactor is sealed and pressurized with carbon monoxide to 750 psi. After 12 h of stirring at 25 °C, the reactor was depressurized and its contents were poured into an ice-cold solution of CH_3OH and Na_2CO_3. Filtration and removal of the solvent gave crude product (**22**), which was further purified by column chromatography.

3.2. Analytical data for new compounds

3.2.1. 4,4′-Dibenzhydryl-[2,2′]bipyridinyl (14). Brown solid, mp 181–187 °C ($CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 5.67 (s, 2H), 7.05 (d, J=3.9 Hz, 2H), 7.18–7.37 (m, J=20 Hz), 8.33 (s, 2H), 8.59 (d, J=4.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 56.6, 122.4, 124.6, 126.8, 128.6, 129.4, 142.2, 149.3, 153.9. HRMS: $C_{36}H_{28}N_2$, calcd 488.225249, found 488.223488.

3.2.2. 2,6-Dibenzhydryl-pyridine (15). Yellow solid, mp 94–101 °C ($CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 5.66 (s, 2H), 7.06 (d, J=7.7 Hz, 2H), 7.28–7.35 (m, 20H), 7.57 (t, J=7.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 59.2, 121.4, 126.4, 128.3, 129.5, 136.9, 143.2, 162.4. MS: 411 (M+), 410, 332, 244, 165. HRMS: $C_{31}H_{25}N$, calcd 411.198700, found 411.198941.

3.2.3. 3-Benzhydryl-5-bromo-pyridine (16). Oil. ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 5.60 (s, 1H), 7.16–7.18 (d, J=7.4 Hz, 2H), 7.28–7.41 (m, 6H), 7.63 (br s, 1H), 8.42 (d, J=1.2 Hz, 1H), 8.62 (d, J=1.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 54.1, 120.8, 127.1, 128.8, 129.3, 139.2, 141.4, 142.0, 148.9, 149.1. MS: 325 (M+), 323, 244, 167. HRMS: $C_{18}H_{14}BrN$, calcd 323.030961, found 323.030937.

3.2.4. 2-Benzhydryl-6-methyl-pyridine (17). White solid, mp 53–58 °C ($CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 2.63 (s, 1H), 5.91 (s, 1H), 6.97 (d, J=7.7 Hz, 1H), 7.02 (d, J=7.7 Hz, 1H), 7.27–7.38 (m, 10H), 7.48–7.51 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 24.6, 59.5, 121.0, 121.3, 126.6, 128.5, 129.6, 136.9, 143.1, 158.0, 162.5. MS: 259 (M^+), 258, 243, 181, 165. HRMS: $C_{19}H_{17}N$, calcd 259.136100, found 259.136453.

3.2.5. 3-Benzhydryl-2-methoxy-pyridine (18). White solid, mp 98–101 °C ($CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 3.94 (s, 3H), 5.85 (s, 1H), 6.86 (dd, J=7.3, 5.0 Hz, 1H), 7.10–7.38 (m, 11H), 8.13 (dd, J=5.0, 1.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 49.7, 53.6, 116.6, 126.4, 126.9, 128.3, 128.8, 129.3, 138.5, 142.8, 144.7, 161.6. MS: 275 (M^+), 260, 242, 184, 167. HRMS: $C_{19}H_{17}NO$, calcd 275.131014, found 275.130983.

3.2.6. 4-(6-Benzhydryl-pyridin-2-yl)-benzoic acid methyl ester (19). White solid, mp 81–85 °C ($CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 4.02 (s, 3H), 5.93 (s, 1H), 7.19–7.21 (m, 1H), 7.33–7.37 (m, 2H), 7.41–7.47 (m, 8H), 7.55–7.58 (m, 1H), 7.69–7.70 (m 2H), 8.18 (d, J=7.7 Hz, 1H), 8.35 (d, J=7.7 Hz, 1H), 8.84 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 52.3, 59.7, 118.2, 122.9, 126.7, 128.1, 128.5, 129.0, 129.6, 130.0, 130.7, 131.6, 137.4, 139.8, 143.3, 155.6, 162.9, 167.1. MS: 379 (M^+), 378, 348, 302, 241, 165. HRMS: $C_{26}H_{21}NO_2$, calcd 379.157229, found 379.157033.

3.2.7. 2-Amino-3-benzhydryl-pyridine (20). White solid, mp 133–135 °C ($CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 4.32 (s, 2H), 5.36 (s, 1H), 6.64 (dd, J=5.0, 7.5 Hz), 6.92 (d, J=7.1 Hz, 1H), 7.14 (d, J=7.1 Hz, 4H), 7.14–7.36 (m, 6H), 8.03 (d, J=4.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 52.2, 114.5, 123.4, 127.1, 128.8, 129.4, 137.6, 141.3, 146.2, 156.6. MS: 260 (M^+), 259, 242, 181, 165. HRMS: $C_{18}H_{16}N_2$, calcd 260.131349, found 260.131390.

3.2.8. 3-Benzhydryl-1-methyl pyridinium triflate (21). White solid, mp 131–133 °C (Hexane–ether). ^{1}H NMR ($CDCl_3$, 500 MHz), δ, ppm: 4.36 (s, 3H), 5.85 (s, 1H), 7.12–7.15 (m, 4H), 7.25–7.29 (m, 2H), 7.31–7.36 (m, 4H), 7.87 (dd, J=6.1, 8.1 Hz, 1H), 8.05 (d, J=8.2 Hz, 1H), 8.53 (s, 1H), 8.81 (d, J=6.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz), δ, ppm: 48.8, 53.4, 120.7 (q, J_{C-F}=320 Hz), 127.7, 129.2, 129.3, 140.0, 143.8, 145.0, 145.3, 146.0. Calcd: C, 58.67; H, 4.43; N, 3.42; found: C, 58.63; H, 4.35; N, 3.40.

3.2.9. 1-Methyl-cyclohexanecarboxylic acid pyridin-4-yl-methyl ester (22). Oil. ^{1}H NMR ($CDCl_3$, 500 MHz), δ, ppm: 1.16 (s, 3H), 1.20–1.56 (m, 8H), 2.00–2.04 (m, 2H), 5.08 (s, 2H), 7.19–7.21 (m, 2H), 8.56 (s, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz), δ, ppm: 23.1, 25.6, 35.4, 43.2, 63.9, 121.8, 145.5, 149.8, 177.2. MS: 233 (M+), 178, 125, 97.

3.2.10. Adamantane-1-carboxylic acid pyridin-4-yl-methyl ester (23). White solid, mp 55–56 °C (hexane–ether). ^{1}H NMR ($CDCl_3$, 500 MHz), δ, ppm: 1.66–1.74 (m, 6H), 1.92 (s, 6H), 1.99–2.03 (m, 3H), 5.09 (s, 2H), 7.23 (d, J=4.4 Hz, 2H), 8.57 (d, J=3.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz), δ, ppm: 27.9, 36.4, 38.8, 40.8, 63.7, 121.7, 146.1, 149.5, 176.9. MS: 271 (M^+), 227, 163, 135, 93.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.04.022.

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