Acid- or base-promoted photostimulated homolytic *tert*-butylation of pyridines and thiophenes

Byeong Hyo Kim,* Insik Jeon, Tae Hee Han, Hae Jin Park and Young Moo Jun

Department of Chemistry, Kwangwoon University, Seoul, 139-701, Korea

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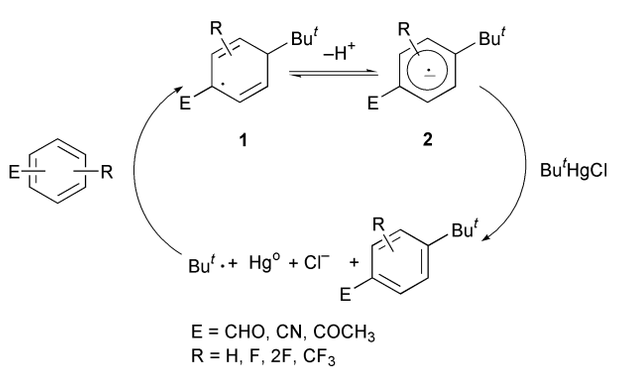
Regioselective photostimulated homolytic *tert*-butylations for heteroaromatics such as pyridines or thiophenes are investigated with *tert*-butylmercury(II) chloride in the presence of toluene-*p*-sulfonic acid (PTSA) or 1,4-diazabicyclo[2.2.2]octane (DABCO) respectively. While the promotion effect of acid is quite strong for basic pyridines, the acid does not promote the reaction effectively for non-basic thiophenes. On the other hand, pyridines and thiophenes exhibit similar tendency for the base-promoted homolytic *tert*-butylations, and the reactivity is mainly controlled by substituent carbonyl or cyano groups as well as by regioselectivity.

Homolytic aromatic substitution has received little attention in the branch of aromatic substitution and this lack of interest was mainly due to the facts that the radical sources were not always easily available, the yields were usually poor, and the isomer selectivity was poor. However, homolytic substitutions with nucleophilic radicals are of considerable importance for protonated heteroaromatic bases, since protonation of heteroaromatics is known to activate them toward radical addition.[1–5] As activation by protonation is needed for the reaction, most of the homolytic substitutions are limited to heteroaromatic bases such as pyridines and quinolines. Therefore the development of homolytic alkylations of non-protonated heteroaromatic bases and homocyclic aromatic substrates was restricted within a narrow range.

Radical chain reactions between alkylmercury(II) halides and heteroaromatics could be utilized as a unique and convenient alkylation methodology. Photolysis of alkylmercury(II) halides has proved to be a convenient method for the generation of alkyl radicals, and these radicals can undergo oxidative (substitutive) homolytic reactions with unsaturated compounds in the presence of a base such as 1,4-diazabicyclo[2.2.2]octane (DABCO).[6–14] Previously reported examples of oxidative alkylations with unsaturated compounds include those of coumarin,[6] maleimide,[7] acyclic 1,4-enediones,[8] 1,4-naphthoquinone,[6] fumaronitrile,[9] 2-substitution in benzothiazole and benzimidazole,[10] electron-deficient arenes,[11] and intramolecular cyclizations leading to α-tetralone.[6,12] We also have reported that bimolecular aromatic homolytic substitutions proceeded in a similar mechanism shown in Scheme 1 in which the substituent E can stabilize the radical adduct **1** and the radical anion **2**.[11,13,14] DABCO can abstract a proton from **1**; consequently, a chain reaction is initiated by electron transfer to Bu^{t}HgCl, regenerating Bu^t·. With this radical chain reaction, we have demonstrated alkylations of fluoro-, trifluoromethyl-, or difluoro-substituted acylbenzenes and benzonitriles *via* radical chain reactions. These were the first examples for that kind of electron-deficient aromatic chemical.[11,14] As the radical chain reaction for the oxidative alkylation works well on electron-deficient aromatics, it is worth exploring a wider range of electron-deficient aromatics such as heteroaromatics that have been rarely investigated previously.



Scheme 1

In this paper we describe an application of the oxidative *tert*-butylation processes through the photolysis of *tert*-butylmercury(II) chloride in the presence of PTSA or DABCO with electron-withdrawing-group-substituted heteroaromatics such as acylpyridines, cyanopyridines, and acylthiophenes.

Results and discussion

Protonation of basic heteroaromatics such as pyridine is known to activate them toward radical additions. We observed the promoting effect of protonation for pyridines, quinolines, and isoquinolines previously.[13] For the generalization of acid- or base-promoted alkylation of heteroaromatic compounds for the broader application, we decided to extend it to acyl- or cyano-substituted heteroaromatic compounds to generalize our radical chain reaction.

For the general homolytic alkylation of protonated heteroaromatic bases, the promoting effect of protonation is apparent only in the initial stages of the reaction. In terms of frontier orbital theory, protonated pyridine has, in fact, considerably lower HOMO and LUMO energies than do normal benzene derivatives. Thus, photolysis of Bu^{t}HgCl with an acylpyridine in the presence of acid such as toluene-*p*-sulfonic acid (PTSA) is expected to lead to the *tert*-butylated acylpyridine since acylpyridines are heteroaromatic bases. Moreover, it might give a chance for alkylation to proceed without the promotion of the acid because the acyl group could lower HOMO and LUMO energies of pyridine that are already lower than that of acylbenzenes.

With this fact in our mind, we tried photostimulated *tert*-butylation in the presence of the proton source PTSA. Thus, photolysis of Bu^{t}HgCl (4 equiv.)–KI (4 equiv.) with pyridine-3-carbaldehyde (1 equiv.) in DMSO in the presence of PTSA (2 equiv.) at 35–40 °C for 7 h yielded 6-(1,1-dimethylethyl)-

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Table 1 Photostimulated reactions of electron-deficient heteroaromatics with Bu^{t}HgCl–PTSA–KI in DMSO[a]

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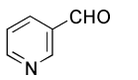
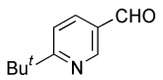
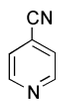
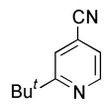
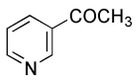
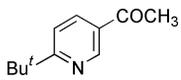
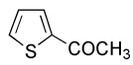
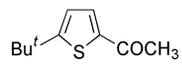
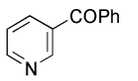
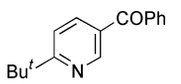
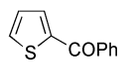
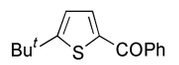
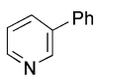
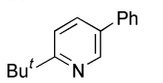
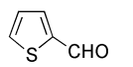
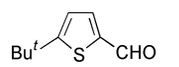
1		7		72	5		24		44[c]
2		7		75	6		24		36[d]
3		6		76	7		24		47[d]
4		6		99	8		24		43[d]

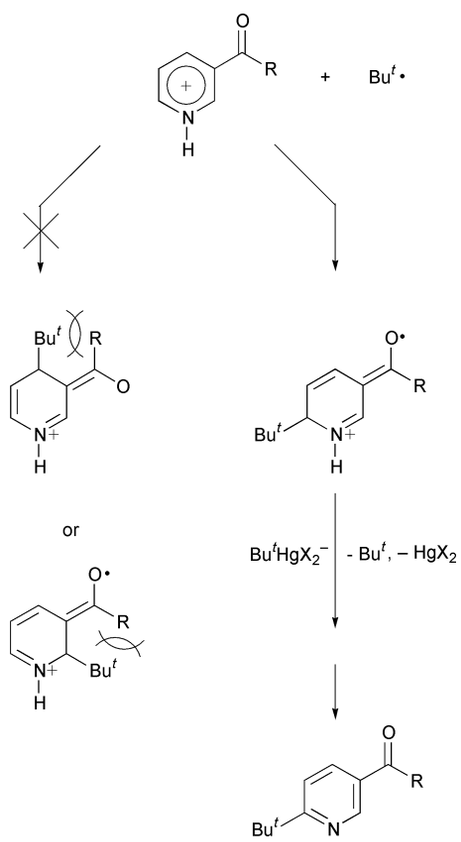
[a] 0.1 M substrate, 0.4 M Bu^{t}HgCl, 0.4 M KI and 0.2 M PTSA were used. [b] GC yield with an internal standard (octane). [c] 40% of di-*tert*-butylated products were obtained [d] Starting substrate was recovered.

pyridine-3-carbaldehyde in 72% (Table 1, entry 1). Without PTSA, the reaction showed poor reactivity and regioselectivity [photolysis of pyridine-3-carbaldehyde (1 equiv.)–Bu^{t}HgCl (6 equiv.)–KI (4 equiv.) in DMSO, 7 h, gave a mixture of two *tert*-butylated products and di-*tert*-butylated product with less than 50% overall]. 3-Phenylpyridine underwent quantitative *tert*-butylation (entry 4), which also suggests that protonation at nitrogen rather than at carbonyl oxygen mainly controls the reaction. It is also worth noting that 4-cyanopyridines reaction with Bu^{t}HgCl–KI–PTSA produced 2-*tert*-butylated product (44%) and 2,6-di-*tert*-butylated product (31%) along with ≈9% of another di-*tert*-butylated product (regioselectivity was not determined) rather than 3-*tert*-butylated product (entry 5). Definitely, protonation on the basic nitrogen in pyridine was activating the pyridine moiety toward radical additions.

Alkyl radical attack occurs selectively at the ring positions that are *ortho* or *para* to the protonated nitrogen atom. The selectivity of this reaction has been attributed to polar effects that operate during the addition step.[15] Furthermore, *ortho* (to the carbonyl) *tert*-butylated products are rarely observed because of formation of a sterically congested *ortho tert*-butylated radical intermediate (Scheme 2). Thus photolysis of Bu^{t}HgCl–KI with 3-acylpyridines or 3-phenylpyridine in the presence of PTSA at 35–40 °C for 6–7 h yielded *tert*-butylated 3-acylpyridines or 3-phenylpyridine regioselectively in reasonable 72–99% yield (entries 1–4).

In contrast, photolysis of Bu^{t}HgCl–KI with thiophenes in the presence of PTSA may not exhibit good results since thiophenes are not basic enough heteroaromatic compounds. As expected, the promoting effect of protonation for thiophenes was not as effective as the pyridine case. Even with an extended reaction time, it produced *tert*-butylated products in 36–47% yield only, along with recovered starting material (entries 6–8).

As the radical chain reaction for the oxidative alkylation under basic conditions works well on electron-deficient aromatics in our preceding experiments,[11,14] we tried *tert*-butylation of pyridines and thiophenes in the presence of DABCO base instead of PTSA. As far as *tert*-butyl radical can attack the aromatic ring to form radical adduct **3**, and provided the carbonyl or cyano group can stabilize the radical adduct **3** and the radical anion **4**, oxidative alkylation would be quite successful. DABCO can abstract a proton from **3**; consequently, a chain reaction is initiated by electron transfer to Bu^{t}HgCl regenerating R$^\bullet$ (Scheme 3).

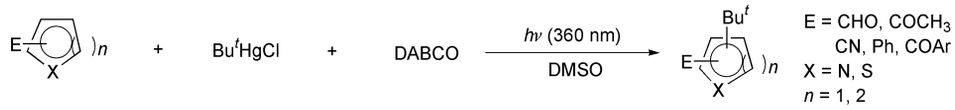


Scheme 2

Photolysis of Bu^{t}HgCl (4 equiv.) in DMSO with pyridine-3-carbaldehyde (Table 2, entry 2) or 3-acetylpyridine (entry 3) in the presence of DABCO (4 equiv.) at 35–40 °C produced oxidative *tert*-butylated product, 6-(1,1-dimethylethyl)pyridine-3-carbaldehyde (89%) or 1-[6-(1,1-dimethylethyl)pyridin-3-yl]ethanone (quantitative yield) respectively as an exclusive product. As anticipated, *ortho tert*-butylated products are rarely observed because of the high energy requirement for formation of the sterically congested *ortho tert*-butylated radical intermediate.

In acid-promoted reaction, *tert*-butyl radical attack occurs selectively at the *ortho* positions to the protonated nitrogen

Table 2 Photostimulated reactions of electron-deficient heteroaromatics with Bu^{t}HgCl–DABCO in DMSO[a]



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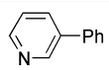
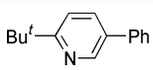
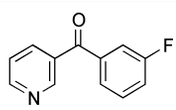
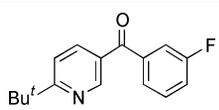
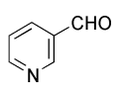
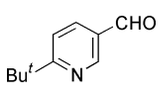
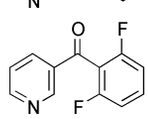
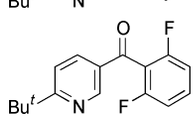
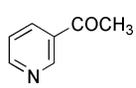
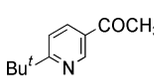
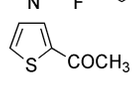
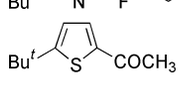
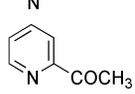
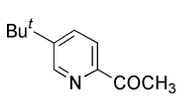
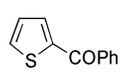
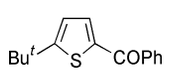
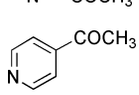
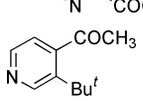
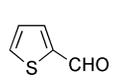
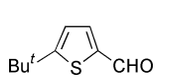
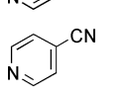
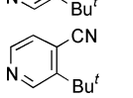
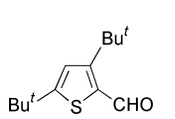
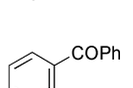
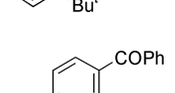
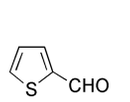
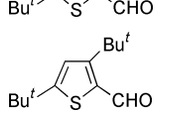
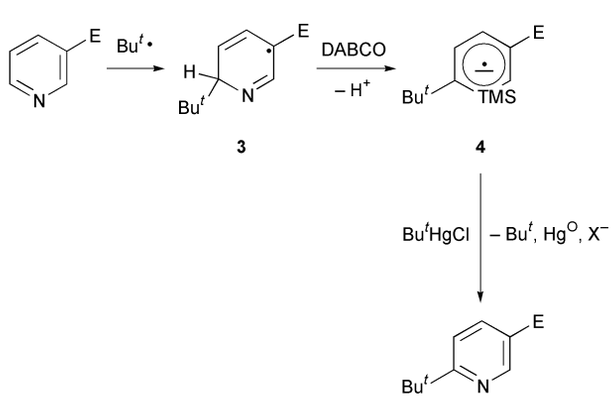
1		96		26	8		6		58
2		18		89	9		6		61
3		24		100 (87)[c]	10		37		69
4		48		62	11		5		69
5		48		tr[d]	12		4.5		48
6		48		70					29
7		6		84	13		44		100 (94)[c]

[a] 0.1 M substrate, 0.4 M Bu^{t}HgCl, and 0.4 M DABCO were used. [b] GC yield with an internal standard (octane). [c] isolated yield. [d] Starting substrate was recovered mostly. Unchanged starting substrates were recovered in all experiments.



E = CHO, COCH$_3$, COAr, CN, Ph

Scheme 3

atom. However, unlike protonated pyridine cases, regioselectivity of the base-promoted reaction was drastically changed. In the case of photolysis of 4-cyanopyridine under basic conditions, it produced 3-(1,1-dimethylethyl)pyridine-4-carbonitrile in 70% yield (Table 2, entry 6). Definitely, regioselectivity was mainly determined by the resonance stabilization of a radical adduct, *i.e. ortho*-, *para*-directing for the *tert*-butyl radical relative to the carbonyl group.

Unlike acid-promoted reactions, thiophenes produced similar yields compared to the pyridine reactions, as the reactivity may be controlled mainly by stability of the heteroaromatic substrate. Results of photostimulated reactions of various pyridines and thiophenes in the presence of DABCO are summarized in Table 2.

Table 3 Relative reactivities of various heteroaromatics towards the *tert*-butyl radical compared with benzaldehyde[a]

Entry	Substrate	Rel. react.[b]
1	2-Acetylpyridine	2.1
2	3-Acetylpyridine	3.7
3	3-Benzoylpyridine	9.4
4	4-Cyanopyridine	9.6
5	2-Acetylthiophene	13
6	2-Benzoylthiophene	16
7	Pyridine-3-carbaldehyde	21
8	Thiophene-2-carbaldehyde	30

[a] Substrate and standard (0.5 mmol each)–Bu^{t}HgCl (3 mmol)–DABCO (3 mmol) in DMSO (10 mL) were irradiated 360 nm [b] As calculated from the observed alkylation products after 2–5 h of irradiation.

In Table 3, the relative reactivities of the oxidative *tert*-butylation of various pyridines and thiophenes are summarized based on product analyses of comparative *tert*-butylations using benzaldehyde as a standard. In general, acylpyridine derivatives are more reactive towards *tert*-butyl radical than are difluoro-substituted acylbenzenes that we have examined previously.[14] Among the compounds that we examined for the base-catalyzed oxidative free-radical chain reaction, thiophene-2-carbaldehyde is the most reactive heteroaromatic compound and the order of reactivity shows benzenes < pyridines < thiophenes. As shown in Table 2, thiophene-2-carbaldehyde produced di-*tert*-butylated compound because it is too reactive to stop the reaction at the stage of mono-*tert*-butylation. In general, thiophenes are relatively more reactive compared with pyridines with respect to base-promoted free-radical chain reactions.

In summary, we have demonstrated acid- or base-catalyzed oxidative *tert*-butylations of acylpyridines, cyanopyridines, and acylthiophenes. The promotion effect of acid was quite strong for basic pyridines; however, the acid did not promote the reaction effectively for non-basic thiophenes. On the other hand, pyridines and thiophenes exhibited similar tendency and reactivity for base-promoted homolytic *tert*-butylations. While the regioselective *ortho* attack of *tert*-butyl group relative to nitrogen in acylpyridines was observed during the acid-catalyzed reaction, the regioselective *para* attack relative to acyl group in acylpyridines was observed in DABCO-promoted reactions.

Experimental

General

Chemical reagents were purchased mostly from Aldrich and the reagents were used without further purification in most cases. Solvents were purchased and dried by usual laboratory techniques.

Analytical gas chromatography (GC) was performed on a Donam 6200 gas chromatograph equipped with DB-1 capillary column and Hitachi D-2500 integrator. ^{1}H NMR spectra were recorded on a 300 MHz Bruker instrument, and ^{13}C NMR spectra were recorded on a 75 MHz Bruker instrument. Chemical shifts are reported in ppm from tetramethylsilane (TMS). High-resolution mass spectra were recorded on a JEOL JMS-DX 303 mass spectrometer. IR were recorded on a Nicolet 205 FT-IR.

Most products were isolated by flash column chromatography on silica gel (230–400 mesh ASTM, purchased from Merck) with eluents of mixed solvents (hexane and ethyl acetate). GC yields were determined by using an internal standard (octane) and were corrected with predetermined response factors.

General procedure for *tert*-butylation of heteroaromatics

In the presence of PTSA. The substrate (1 mmol), Bu^{t}HgCl (4 mmol), KI (4 mmol), and PTSA (2 mmol) were dissolved in 10 mL of DMSO in a flame-dried Pyrex test tube under a nitrogen atmosphere and irradiated with a UV lamp (360 nm) in a Rayonet photoreactor. Work-up involved treatment with 50 mL of aq. $Na_2S_2O_3$, neutralization if required, and extraction with diethyl ether. The combined extracts were washed with brine. After drying over $MgSO_4$ and evaporation of the solvent, the GC yield was determined with an internal standard (octane) and, if necessary, the products were isolated by flash column chromatography using ethyl acetate–hexane as the eluent.

In the presence of DABCO. The substrate (1 mmol), Bu^{t}HgCl (4 mmol), and DABCO (4 mmol) were dissolved in 10 mL of DMSO in a flame-dried Pyrex test tube under a nitrogen atmosphere and irradiated with a UV lamp (360 nm) in a Rayonet photoreactor. Work-up involved treatment with 50 mL of aq. $Na_2S_2O_3$ followed by diethyl ether extraction and washing of the organic layer with brine. After drying over $MgSO_4$ and evaporation of the solvent, the GC yield was determined with an internal standard (octane) and, if necessary, the products were isolated by flash column chromatography using ethyl acetate–hexane as the eluent.

General procedure for the competition reaction

The substrate (0.5 mmol) and benzaldehyde (0.5 mmol, standard), Bu^{t}HgCl (3 mmol), and DABCO (3 mmol) were dissolved in 10 mL of deoxygenated DMSO in a flame-dried Pyrex tube under a nitrogen atmosphere and irradiated with 360 nm in a Rayonet photoreactor. Before the reaction was completed (usually 2–5 h), the mixture was quenched with aq. $Na_2S_2O_3$ and extracted with diethyl ether. The extract was washed three times with aq. $Na_2S_2O_3$ dried over $MgSO_4$, and evaporated. Relative ratio of *tert*-butylated arenes was determined by GC with an internal standard (octane) and the relative reactivity was calculated based on the ratio of product formation and/or remaining substrate/benzaldehyde.

6-(1,1-Dimethylethyl)pyridine-3-carbaldehyde. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.53; ν_{max}/cm^{-1} 3051 (aromatic CH), 2959 (aliphatic CH), 2846 (aldehyde CH), 2747 (aldehyde CH), 1709 (CO), 1597, 1424; δ_H (300 MHz; $CDCl_3$) 1.41 (9H, s, Bu^t), 7.53 (1H, d, *J* 8.2 Hz, aromatic), 8.12 (1H, dd, *J* 1.9, 8.2 Hz, aromatic), 9.02 (1H, d, *J* 1.9 Hz, aromatic), 10.09 (1H, s, aldehyde); δ_C (75 MHz; $CDCl_3$) 190.56, 175.51, 151.27, 135.89, 128.93, 119.52, 38.15, 29.81; *m*/*z* 163.0996 ($C_{10}H_{13}NO$ requires M_r, 163.0997).

1-[6-(1,1-Dimethylethyl)pyridin-3-yl]ethanone. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.54; ν_{max}/cm^{-1} 3031 (aromatic CH), 2963 (aliphatic CH), 1699 (CO), 1598, 1493, 1136; δ_H (300 MHz; $CDCl_3$) 1.30 (9H, s, Bu^t), 2.53 (3H, s, acetyl), 7.37 (1H, d, *J* 8.3 Hz, aromatic), 8.08 (1H, d, *J* 8.3 Hz, aromatic), 9.03 (1H, s, aromatic); δ_C (75 MHz; $CDCl_3$) 196.57, 174.00, 149.01, 135.76, 129.62, 119.05, 37.90, 29.87, 26.57; *m*/*z* 117.1154 ($C_{11}H_{15}NO$ requires M_r, 177.1154).

1-[5-(1,1-Dimethylethyl)pyridin-2-yl]ethanone. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.68; ν_{max}/cm^{-1} 3064 (aromatic CH), 2968 (aliphatic CH), 1702 (CO), 1596, 1482; δ_H (300 MHz; $CDCl_3$) 1.35 (9H, s, Bu^t), 2.68 (3H, s, methyl), 7.78 (1H, dd, *J* 2.4, 8.2 Hz, aromatic), 7.95 (1H, d, *J* 8.2 Hz, aromatic), 8.70 (1H, d, *J* 2.4 Hz, aromatic); δ_C (75 MHz; $CDCl_3$) 199.92, 151.11, 150.09, 146.67, 133.62, 121.20, 34.01, 30.79, 25.76; *m*/*z* 117.1159 ($C_{11}H_{15}NO$ requires M_r, 177.1154).

3-(1,1-Dimethylethyl)pyridine-4-carbonitrile. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.32; ν_{max}/cm^{-1} 3052 (aromatic CH), 2981 (aliphatic CH), 2237 (conj. CN), 1587, 1484; δ_H (300 MHz; $CDCl_3$) 1.54 (9H, s, Bu^t), 7.52 (1H, d, *J* 4.7 Hz, aromatic), 8.61 (1H, d, *J* 4.7 Hz, aromatic), 8.82 (1H, s, aromatic); δ_C (75 MHz; $CDCl_3$) 148.41, 147.82, 146.15, 127.56, 118.62, 117.76, 34.67, 29.87; *m*/*z* 160.1002 ($C_{10}H_{12}N_2$ requires M_r, 160.1001).

2-(1,1-Dimethylethyl)pyridine-4-carbonitrile. White solid; mp 54–55 °C; TLC (20% ethyl acetate–hexane) R_f 0.49; ν_{max}/cm^{-1} 3059 (aromatic CH), 2967 (aliphatic CH), 2236 (conj. CN), 1604, 1486; δ_H (300 MHz; $CDCl_3$) 1.31 (9H, s, Bu^t), 7.25 (1H, d, *J* 4.8 Hz, aromatic), 7.49 (1H, s, aromatic), 8.66 (1H, d, *J* 4.8 Hz, aromatic); δ_C (75 MHz; $CDCl_3$) 171.06, 149.59, 122.02, 120.99, 120.43, 117.06, 37.87, 29.82; *m*/*z* 160.1018 ($C_{10}H_{12}N_2$ requires M_r, 160.1001).

2,6-Bis(1,1-dimethylethyl)pyridine-4-carbonitrile. Colorless liquid; TLC (20% ethyl acetate–hexane) R_f 0.61; ν_{max}/cm^{-1} 3054 (aromatic CH), 2963 (aliphatic CH), 2239 (conj. CN), 1598, 1469; δ_H (300 MHz; $CDCl_3$) 1.28 (18H, s, Bu^t), 7.24 (2H, s, aromatic); δ_C (75 MHz; $CDCl_3$) 169.14, 120.15, 117.80, 117.31, 38.04, 29.86; *m*/*z* 216.1629 ($C_{14}H_{20}N_2$ requires M_r, 216.1626).

5-(1,1-Dimethylethyl)thiophene-2-carbaldehyde. Colorless liquid; TLC (20% ethyl acetate–hexane) R_f 0.60; ν_{max}/cm^{-1} 3077 (aromatic CH), 2968 (aliphatic CH), 2876 (aldehyde CH), 2748 (aldehyde CH), 1678 (CO), 1483; δ_H (300 MHz; $CDCl_3$) 1.40 (9H, s, Bu^t), 6.96 (1H, d, *J* 3.9 Hz, aromatic), 7.60 (1H, d, *J* 3.9 Hz, aromatic), 9.81 (1H, s, aldehyde); δ_C (75 MHz; $CDCl_3$) 182.86, 169.05, 140.81, 136.78, 123.18, 35.29, 32.04; *m*/*z* 168.0605 ($C_9H_{12}OS$ requires M_r, 168.0609).

3,5-Bis(1,1-dimethylethyl)thiophene-2-carbaldehyde. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.75; ν_{max}/cm^{-1}

3054 (aromatic CH), 2957 (aliphatic CH), 2870 (aldehyde CH), 2732 (aldehyde CH), 1658 (CO), 1476; δ_H (300 MHz; $CDCl_3$) 1.36 (9H, s, Bu^t), 1.45 (9H, s, Bu^t), 6.83 (1H, s, aromatic), 10.28 (1H, s, aldehyde); δ_C (75 MHz; $CDCl_3$) 182.97, 166.50, 160.21, 135.47, 124.24, 35.28, 35.14, 33.06, 31.89; *m*/*z* 224.1234 ($C_{13}H_{20}OS$ requires M_r, 224.1235).

1-[5-(1,1-Dimethylethyl)-2-thienyl]ethanone. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.60; ν_{max}/cm^{-1} 3049 (aromatic CH), 2934 (aliphatic CH), 1670 (CO), 1599, 1445; δ_H (300 MHz; $CDCl_3$) 1.35 (9H, s, Bu^t), 2.47 (3H, s, acetyl), 6.83 (1H, d, *J* 3.8 Hz, aromatic), 7.49 (1H, d, *J* 3.8 Hz, aromatic); δ_C (75 MHz; $CDCl_3$) 190.74, 167.35, 141.23, 132.63, 122.86, 35.16, 32.13, 26.45; *m*/*z* 182.0767 ($C_{10}H_{14}OS$ requires M_r, 182.0765).

2-(1,1-Dimethylethyl)-5-phenylpyridine. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.75; ν_{max}/cm^{-1} 3034 (aromatic CH), 2964 (aliphatic CH), 1599, 1486, 760, 703; δ_H (300 MHz; $CDCl_3$) 1.40 (9H, s, Bu^t), 7.34–7.47 (4H, m, aromatic), 7.54–7.58 (2H, m, aromatic), 7.79 (1H, dd, *J* 2.0, 8.3 Hz, aromatic), 8.79 (1H, d, *J* 2.0 Hz, aromatic); δ_C (75 MHz; $CDCl_3$) 168.17, 146.97, 138.02, 134.56, 133.45, 128.96, 127.66, 126.95, 118.94, 37.19, 30.19; *m*/*z* 211.1362 ($C_{15}H_{17}N_1$ requires M_r, 211.1361).

[6-(1,1-Dimethylethyl)pyridin-3-yl]phenylmethanone. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.62; ν_{max}/cm^{-1} 3053 (aromatic CH), 2957 (aliphatic CH), 1666 (CO), 1595, 1484, 1306; δ_H (300 MHz; $CDCl_3$) 1.40 (9H, s, Bu^t), 7.46–7.60 (4H, m, aromatic), 7.81 (2H, d, *J* 8.3 Hz, aromatic), 8.06 (1H, dd, *J* 2.2, 8.3 Hz, aromatic), 8.94 (1H, d, *J* 2.2 Hz, aromatic); δ_C (75 MHz; $CDCl_3$) 194.77, 173.26, 150.02, 137.63, 136.94, 132.80, 130.20, 129.87, 128.42, 118.84, 37.89, 29.93; *m*/*z* 239.1316 ($C_{16}H_{17}NO$ requires M_r, 239.1310).

[6-(1,1-Dimethylethyl)pyridin-3-yl](3-fluorophenyl)methanone. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.68; ν_{max}/cm^{-1} 3051 (aromatic CH), 2967 (aliphatic CH), 1674 (CO), 1590, 1451, 1300, 860, 792, 704; δ_H (300 MHz; $CDCl_3$) 1.38 (9H, s, Bu^t), 7.25–7.32 (1H, m, aromatic), 7.42–7.57 (4H, m, aromatic), 8.04 (1H, dd, *J* 2.2, 8.3 Hz, aromatic), 8.91 (1H, d, *J* 2.2 Hz, aromatic); δ_C (75 MHz; $CDCl_3$) 193.52, 173.83, 164.21, 160.92, 150.09, 139.13, 139.04, 137.51, 130.21, 130.11, 129.73, 125.73, 125.69, 119.99, 119.71, 118.95, 116.72, 116.42, 38.01, 29.95; *m*/*z* 257.1207 ($C_{16}H_{16}FNO$ requires M_r, 257.1216).

(2,6-Difluorophenyl)[6-(1,1-dimethylethyl)pyridin-3-yl]-methanone. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.63; ν_{max}/cm^{-1} 3070 (aromatic CH), 2965 (aliphatic CH), 1678 (CO), 1630, 1596, 1470, 1287, 791, 704; δ_H (300 MHz; $CDCl_3$) 1.36 (9H, s, Bu^t), 6.97 (2H, t, *J* 7.7 Hz, aromatic), 7.39–7.49 (2H, m, aromatic), 8.11 (1H, dd, *J* 2.2, 8.3 Hz, aromatic), 8.88 (1H, br s, aromatic); δ_C (75 MHz; $CDCl_3$) 187.48, 174.99, 161.45, 161.34, 158.11, 158.01, 150.51, 136.69, 132.47, 132.36, 132.20, 129.50, 119.26, 112.14, 111.81, 38.15, 29.86; *m*/*z* 275.1128 ($C_{16}H_{15}F_2NO$ requires M_r, 275.1122).

[5-(1,1-Dimethylethyl)-2-thienyl]phenylmethanone. Colorless liquid; TLC (30% ethyl acetate–hexane) R_f 0.61; ν_{max}/cm^{-1} 3056 (aromatic CH), 2954 (aliphatic CH), 1635 (CO), 1532, 1453; δ_H (300 MHz; $CDCl_3$) 1.40 (9H, s, Bu^t), 6.88 (1H, d, *J* 4.0 Hz, aromatic), 7.42–7.47 (3H, m, aromatic), 7.51–7.56 (1H, m, aromatic), 7.81 (2H, d, *J* 7.0 Hz, aromatic); δ_C (75 MHz; $CDCl_3$) 188.07, 167.70, 140.20, 138.16, 135.15, 131.82, 128.90, 128.20, 122.81, 35.12, 32.05; *m*/*z* 244.0922 ($C_{15}H_{16}OS$ requires M_r, 244.0922).

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