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Halogenation of Pyrazoles Using *N*-Halosuccinimides in CCl_4 and in Water

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Abstract: Reaction of pyrazoles with *N*-halosuccinimides (NXS, X = Br, Cl) in either CCl_4 or water gave 4-halopyrazoles in excellent yields. The reaction was carried out under mild conditions and did not require any catalysts or special precautions. The reaction provides an efficient method for 4-C halogenation of pyrazoles.

Keywords: carbon tetrachloride, halogenation, *N*-halosuccinimides, pyrazoles, water

INTRODUCTION

A large number of compounds with important biological and pharmaceutical activities contain key substructures of 4-halopyrazoles.[1,2] 4-Halopyrazoles have also been used in the synthesis of biologically active compounds and cross-coupling reactions such as the Suzuki reaction,[3–5] Heck reaction,[1,6] Sonogashira reaction,[2,7] and other important reactions.[8] 4-Halopyrazoles are usually prepared by halogenation of pyrazoles using various halogenating agents such as Cl_2, HOCl, Br_2, KI/KIO_3, ICl, I_2/$PhI(OAc)_2$, and $KICl_2$.[9] *N*-Halosuccinimides (NXS) have also been used in the halogenations of pyrazoles.[1,6,10] However, as indicated by H. A. Stefani et al., the examination of previously reported methods reveals serious synthetic drawbacks, such as mixture of products, long reaction times, high temperatures, and use of catalysts.[11] Recently, Stefani and coworkers reported the halogenation of pyrazoles using NXS under ultrasound irradiation, giving 4-halopyrazoles in

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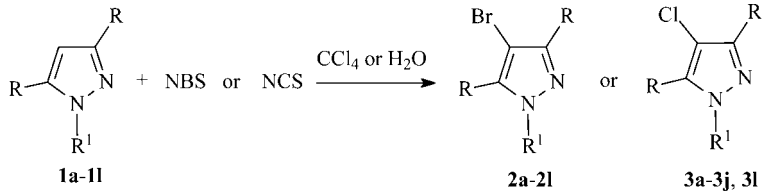
good yields.[11] These halogenation reactions using NXS are usually carried out in organic solvents and require an excessive quantity of NXS and an N_2 atmosphere.[1,6,10,11] Here we report a highly efficient and convenient halogenation reaction of pyrazoles using NXS without the need for any catalysts and protection from oxygen and water.

RESULTS AND DISCUSSION

Reaction of pyrazoles **1** and NXS, (X = Br, Cl) in CCl_4 or water at the appropriate temperature and time afforded 4-bromopyrazoles **2** or 4-cholopyrazoles **3** (Scheme 1). Most reactions gave excellent yields (Table 1). Many of the reactions could be completed in a short time (0.5–2 h; see Table 1) at room temperature or a little higher temperature depending on the reactivity of the substrates. Enhancing the reaction temperature could obviously accelerate the reactions. For example, reaction of N-bromosuccinimide (NBS) with **1a**, **1c**, **1e** and **1f** at 25°C could be completed in 0.5–1 h. However, if the temperature was enhanced to 35°C, the reaction could be complete in about 15 min. These reactions did not need the existence of catalysts and an N_2 atmosphere. They went along well in either CCl_4 or water (distilled water or tap water). Actually the reaction could also proceed well in other organic solvents. We examined the reaction of **1c** with NBS in various organic solvents, including $CHCl_3$, CH_2Cl_2, CH_3COOEt, THF, and EtOH. In each case, the reaction gave **2c** in 90–95% yield. In most reactions that we studied, H_2O is superior to CCl_4. The reactions carried out in water often exhibited a higher reaction rate and required lower reaction temperature and shorter reaction time. In some cases, the reaction could only proceed in water. For example, reaction of N-chlorosuccinmide (NCS) with **1i** could not proceed in CCl_4 even under refluxing conditions, while in water the reaction could be completed at 80°C (bath temperature) in 2 h. A similar result was also observed in the reaction of **1k** with NBS.

The activity of the pyrazoles and NXS greatly affects the halogenation reactions. NBS was more active than NCS in the reactions. For instance,



Scheme 1. **a:** R = R^1 = H; **b:** R = H, R^1 = Me; **c:** R = Me, R^1 = H; **d:** R = R^1 = Me; **e:** R = Me, R^1 = Ph; **f:** R = Me, R^1 = *o*-MeC_6H_4; **g:** R = Me, R^1 = *o*-$NO_2C_6H_4$; **h:** R = Me, R^1 = 2-(6-MeC_5H_3N); **i:** R = Me, R^1 = PhCO; **j:** R = Ph, R^1 = H; **k:** R = Ph, R^1 = *o*-$NO_2C_6H_4$; **l:** R = *t*-Bu, R^1 = H.

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Table 1. Reaction of pyrazoles with NXS (X = Cl, Br) in CCl_4 or in H_2O

Entry	Starting material	NXS (equiv)	Solvent	Temp (°C)[a]	Time (h)	Product	Yield (%)
1	**1a**	NBS (1.0)	CCl_4	25	2	**2a**	98
2	**1a**	NBS (1.0)	H_2O	25	0.5	**2a**	98
3	**1a**	NCS (1.0)	CCl_4	25	2	**3a**	98
4	**1a**	NCS (1.0)	H_2O	25	3	**3a**	80
5	**1b**	NBS (1.0)	CCl_4	25	2	**2b**	96
6	**1b**	NBS (1.0)	H_2O	25	1	**2b**	96
7	**1b**	NCS (1.0)	CCl_4	25	2	**3b**	92
8	**1b**	NCS (1.0)	H_2O	50	6	**3b**	85
9	**1c**	NBS (1.0)	CCl_4	25	2	**2c**	99
10	**1c**	NBS (1.0)	H_2O	25	0.5	**2c**	97
11	**1c**	NCS (1.0)	CCl_4	25	1	**3c**	99
12	**1c**	NCS (1.0)	H_2O	25	1	**3c**	96
13	**1d**	NBS (1.0)	CCl_4	25	2	**2d**	99
14	**1d**	NBS (1.0)	H_2O	25	2	**2d**	96
15	**1d**	NCS (1.0)	CCl_4	50	1	**3d**	99
16	**1d**	NCS (1.0)	H_2O	25	2	**3d**	95
17	**1e**	NBS (1.0)	CCl_4	25	2	**2e**	99
18	**1e**	NBS (1.0)	H_2O	25	2	**2e**	99
19	**1e**	NCS (1.0)	CCl_4	50	1	**3e**	99
20	**1e**	NCS (1.0)	H_2O	50	2	**3e**	98
21	**1f**	NBS (1.0)	CCl_4	25	2	**2f**	99
22	**1f**	NBS (1.0)	H_2O	25	2	**2f**	99
23	**1f**	NCS (1.0)	CCl_4	25	2	**3f**	97
24	**1f**	NCS (1.0)	H_2O	25	2	**3f**	97
25	**1g**	NBS (1.0)	CCl_4	25	3	**2g**	99
26	**1g**	NBS (1.0)	H_2O	25	2	**2g**	99
27	**1g**	NCS (1.0)	CCl_4	80	3	Mixture	—
28	**1g**	NCS (1.0)	H_2O	70	2	**3g**	97
29	**1h**	NBS (1.0)	CCl_4	50	2	**2h**	99
30	**1h**	NBS (1.0)	H_2O	25	0.5	**2vh**	98
31	**1h**	NCS (1.0)	CCl_4	60	2	**3h**	96
32	**1h**	NCS (1.0)	H_2O	60	2	**3h**	95
33	**1i**	NBS (1.0)	CCl_4	90	7	Mixture	—
34	**1i**	NBS (1.0)	H_2O	80	2	**2i**	98
35	**1i**	NCS (1.0)	CCl_4	90	12	NR[b]	—
36	**1i**	NCS (1.5)	H_2O	80	2	**3i**	97
37	**1j**	NBS (1.0)	CCl_4	50	3	**2j**	98
38	**1j**	NBS (1.0)	H_2O	50	3	**2j**	98
39	**1j**	NCS (1.0)	CCl_4	70	3	**3j**	98
40	**1j**	NCS (2.0)	H_2O	80	5	**3j**	97
41	**1k**	NBS (1.0)	CCl_4	90	12	NR[b]	—

(*continued*)

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Table 1. Continued

Entry	Starting material	NXS (equiv)	Solvent	Temp (°C)[a]	Time (h)	Product	Yield (%)
42	**1k**	NBS (1.0)	H_2O	110	12	**2k**	98
43	**1k**	NCS (1.0)	CCl_4	90	12	NR[b]	—
44	**1k**	NCS (1.0)	H_2O	110	12	NR[b]	—
45	**1l**	NBS (1.0)	CCl_4	35	3	**2l**	99
46	**1l**	NBS (1.0)	H_2O	35	3	**2l**	99
47	**1l**	NCS (1.0)	CCl_4	70	2	**3l**	99
48	**1l**	NCS (1.0)	H_2O	70	3	**3l**	98

[a]Bath temperature.
[b]NR = no reaction.

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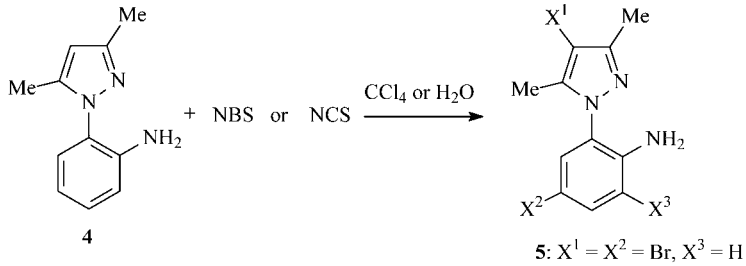
reaction of **1g** with NBS in water could proceed at room temperature very well, whereas the reaction with NCS occurred at 70°C. The activity of pyrazoles was affected by the substituted groups attached on the pyrazole rings. 3,5-Diphenylpyrazoles exhibited obviously less reactivity than pyrazoles or 3,5-dimethylpyrazoles. This can be proved by comparing the reactivity of 3,5-diphenylpyrazole with 3,5-dimethylpyrazole toward NXS. Reaction of the former with NBS in water was completed at 50°C in 3 h (entry 38 in Table 1), whereas the reaction of the latter with NBS in water can be completed at room temperature in 30 min (entry 10 in Table 1). 3,5-Di-*t*-butylpyrazole also showed less reactivity than 3,5-dimethylpyrazole. This is ascribed to steric hindrance of *t*-butyl groups. *N*-Substituted groups on the pyrazole rings also greatly affect the reactivity of pyrazoles. Electron-withdrawing groups obviously decrease the activity of the pyrazoles in the halogenation reactions. For example, reaction of **1i** with NBS in CCl_4 gave a mixture under refluxing conditions, and no reaction occurred even with NCS under refluxing for 12 h in CCl_4 (entry 35 in Table 1). Pyrazoles **1g**, **1h**, and **1k** showed similar reactivity.

The reactions listed in Table 1 usually required only an equivalent of NXS. However, chloronation of **1i** and **1j** in H_2O required 1.5 and 2 equivalent of NCS, respectively. Otherwise, only a mixture was obtained. In addition, we also found that the product of reaction of **1a** with 2 equivalent of NBS was still **2a**.

Compound **4** showed different reactivity from those pyrazoles mentioned previously (Scheme 2 and Table 2). Compound **4** reacted with an equivalent of NBS to afford a mixture containing compound **5**, the starting material, and an unidentified species either in CCl_4 or in water. Treatment of **4** with 2 equiv of NBS in CCl_4 gave the single compound **5**, whereas a similar reaction in water formed a mixture. Use of 3 equivalent of NBS in the reaction led to formation of compound **6** both in CCl_4 and in water. Reaction of **4** with NCS in a different ratio in water always gave a mixture. The products of the reaction in CCl_4 depend on the ratio of **4** to NCS:1:1 ratio gives an unidentified



4

5: $X^1 = X^2 = Br$, $X^3 = H$
6: $X^1 = X^2 = X^3 = Br$
7: $X^1 = X^2 = Cl$, $X^3 = H$
8: $X^1 = X^3 = Cl$, $X^2 = H$
9: $X^1 = X^2 = X^3 = Cl$

Scheme 2.

mixture, 1:2 ratio forms a mixture of **7**, **8**, and minor impurities, and 1:3 ratio produces compound **9** with minor impurities. These are ascribed to the activation of amino group to the phenyl ring.

The separation of the products is usually simple. When CCl_4 was used as the solvent, after filtrating off the by-product, succinimide, the filtrate was washed with water and then dried. The product was obtained by removing the solvent under reduced pressure. When water was used as the solvent, the solid product was isolated by simple filtration, and the liquid product was obtained by extracting with CCl_4. However, solid products such as **2a** and **2b** are soluble in water. They were isolated by extracting with CCl_4. Some products such as **2c** are partly soluble in water. This requires that less

Table 2. Halogenations of **4** with NXS (X = Cl, Br) in CCl_4 or H_2O

Entry	NXS (equiv)	Solvent	Temp. (°C)[a]	Time (h)	Product	Yield (%)
1	NBS (1.0)	CCl_4	25	2	Mixture	—
2	NBS (1.0)	H_2O	25	2	Mixture	—
3	NBS (2.0)	CCl_4	25	2	**5**	98
4	NBS (2.0)	H_2O	25	3	Mixture	—
5	NBS (3.0)	CCl_4	25	8	**6**	97
6	NBS (3.0)	H_2O	25	5	**6**	95
7	NCS (1.0)	CCl_4	25	6	Mixture	—
8	NCS (1.0)	H_2O	25	6	Mixture	—
9	NCS (2.0)	CCl_4	40	2	**7** + **8**	—
10	NCS (2.0)	H_2O	25	6	Mixture	—
11	NCS (3.0)	CCl_4	40	3	**9**	85[a]
12	NCS (3.0)	H_2O	25	8	Mixture	—

[a]Bath temperature.

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water was applied as solvent and to wash the products. Otherwise, the yields were obviously decreased. When we ran the reaction of **1c** with NBS in the usual amount of water and washed the product as usual, only 85% yield of **2c** was obtained.

CONCLUSIONS

In summary, a convenient and highly efficient method of halogenation of pyrazoles using NXS (X = Br, Cl) has been achieved. The reactions can be carried out in CCl_4 or in water, without the need for any protection from air. Water was proved to be excellent solvent in the reactions, exhibiting a higher reaction rate than in CCl_4 and convenient product isolation. The effects of the substituted groups on the pyrazoles are discussed. The pyrazoles with electron-withdrawing groups showed obviously less reactivity. The reactions can usually be completed using an equivalent of NXS, except for the reactions of NCS with **1i** and **1j**, respectively, in water, which required more than 1 equivalent of NXS. We also found that the reaction of 2-(3,5-dimethylpyrazol-1-yl)aniline with NXS (X = Br, Cl) always gave di- or trihalogenated compounds depending on the ratio of the reactants.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded on a Bruker AV300 spectrometer, and the chemical shifts are referenced to internal solvent resonances. IR spectra were recorded on a Bruker Vector-22 spectrometer. Elemental analyses (for the new compounds) were performed by the Analytical Centre of the University of Science and Technology of China. The starting materials **1b–1g, 1i**, **1j**, **1k, 1l**, and **4** were prepared according to the procedures described in the literature.[12–16] Compound **1h** was prepared by refluxing a mixture of 2-hydrazino-6-methyl- pyridine and acetyl acetone in acetic acid. Other regents and solvents were obtained from commercial suppliers.

General Procedure of Halogenations of Pyrazoles in CCl_4

A mixture of appropriate pyrazole (4 mmol) and NXS (see Tables 1 and 2) in CCl_4 (8 mL) was stirred at an appropriate temperature and time. The progress of the reaction was monitored by thin-layer chromatography (TLC) or the disappearance of the NXS at the bottom of the flask. The by-product succinimide was filtered off and washed with CCl_4 (5 mL). The filtrate was washed with water (2 × 10 mL) and dried with $MgSO_4$. The solvent was removed under reduced pressure. The products were obtained in good purity indicated by ^1H NMR spectra.

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General Procedure of Halogenations of Pyrazoles in H_2O

A mixture of appropriate pyrazole (4 mmol) and NXS (see Table 1 and Table 2) in H_2O (5 mL) was stirred at appropriate temperature and time. The progress of the reaction was monitored by TLC or the ^1H NMR spectra of the product (the disappearance of the signal of the CH of the pyrazole ring).

For oily and water-soluble solid products, the reaction mixture was extracted with CCl_4 (2×5 mL) and the extract was dried with $MgSO_4$. The solvent was removed under reduced pressure. The 4-halopyrazoles were obtained in good purity as indicated by ^1H NMR spectra.

For other solid products, the precipitate was collected by filtration, washed with water (2×8 mL), and dried in air. The products so obtained were in good purity as indicated by ^1H NMR spectra.

The samples for elemental analysis were purified by recrystallizing from appropriate solvents (for the solid samples) or by column chromatography (for the liquid samples).

Characterization of the Products

2a: Colorless crystals, mp: 98–100°C (lit.:[17] 96–97°C). ^1H NMR (300 MHz, $CDCl_3$): δ 7.53 (s, 2H, CH), 10.10 (s, 1H, NH).

3a: Colorless crystals, mp: 75–76°C (lit.:[18] 76–77°C). ^1H NMR (300 MHz, $CDCl_3$): δ 7.55 (s, 2H, CH), 10.39 (b, 1H, NH).

2b: Red oil. ^1H NMR (300 MHz, $CDCl_3$): δ 3.82 (s, 3H, CH_3), 7.31 (s, 1H, CH), 7.37 (s, 1H, CH).

3b: Yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 3.78 (s, 3H, CH_3), 7.26 (s, 1H, CH), 7.32 (s, 1H, CH).

2c: Colorless crystal, mp: 123 − 124°C (lit.:[19] 123–124°C). ^1H NMR (300 MHz, $CDCl_3$): δ 2.26 (s, 6H, CH_3), 9.28 (b, 1H, NH).

3c: Colorless crystals, mp: 117 − 118°C (lit.:[20] 117.5–118.5°C). ^1H NMR (300 MHz, $CDCl_3$): δ 2.25 (s, 6H, CH_3).

2d: Yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 2.21 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 3.75 (s, 3H, CH_3).

3d: Light yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 2.13 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 3.65 (s, 3H, CH_3).

2e: Yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 2.31 (s, 6H, CH_3), 7.38–7.50 (m, 5H, Ph).

3e: Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.30 (s, 6H, CH_3), 7.37–7.47 (m, 5H, Ph).

2f: Red orange oil. Anal. calc. for $C_{12}H_{13}BrN_2$: C, 54.36%; H, 4.94%; N, 10.56%; found: C, 54.44%; H, 5.00%; N, 10.40%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.98 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 7.09–7.28 (m, 4H, C_6H_4). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 10.70, 12.42, 17.25, 94.57, 126.63, 127.79, 129.36, 131.02, 136.08, 138.40, 138.67, 147.05. IR (KBr): ν (cm^{-1}) 3067w, 2919m, 2855w, 1631w, 1606w, 1585w, 1546m, 1502vs, 1466m, 1372m, 1289w, 1270w, 1122w, 1078s, 1046m, 1028m, 943w, 816w, 779m, 763s, 721s, 671w, 605w.

3f: Yellow orange oil. Anal. calc. for $C_{12}H_{13}ClN_2$: C, 65.31%; H, 5.94%; N, 12.69%; found: C, 65.69%; H, 5.56%; N, 12.34%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.97 (s, 6H, CH_3), 2.21 (s, 3H, CH_3), 7.09–7.30 (m, 4H, C_6H_4). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 9.83, 11.49, 17.28, 108.27, 126.67, 127.87, 129.38, 131.07, 136.18, 136.66, 138.61, 145.57. IR (KBr): ν (cm^{-1}) 3062w, 3030w, 2957m, 2925m, 2860w, 1607w, 1585w, 1558m, 1504vs, 1473m, 1381m, 1293w, 1272w, 1097s, 1032m, 985w, 945w, 818w, 779m, 763s, 722m.

2g: Yellow powder, mp: 103–104°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.12 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 7.40 (d, 1H, $J = 7.2$ Hz, C_6H_4), 7.52–7.56 (m, 1H, C_6H_4), 7.63–7.68 (m, 1H, C_6H_4), 7.93−7.97 (m, 1H, $J = 8.0$ Hz, C_6H_4).

3g: Yellow powder, mp: 97–98°C. Anal. calc. for $C_{11}H_{10}ClN_3O_2$: C, 52.50%; H, 4.01%; N, 16.70%; found: C, 52.08%; H, 3.93%; N, 16.76%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.11 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 7.40 (d, 1H, $J = 7.8$ Hz, C_6H_4), 7.54 (t, 1H, $J = 7.5$ Hz, C_6H_4), 7.66 (t, 1H, $J = 7.5$ Hz, C_6H_4), 7.95 (m, 1H, Ph). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 9.96, 11.45, 110.18, 125.34, 129.47, 129.81, 132.92, 133.46, 137.39, 146.30, 147.62. IR (KBr): ν (cm^{-1}) 3086w, 2987w, 2925w, 2875w, 1608m, 1587w, 1532s, 1507s, 1452m, 1418m, 1384m, 1359s, 1230m, 1257w, 1113m, 1090m, 1028m, 956w, 852m, 802w, 780m, 752m, 703m, 661w, 635w, 587w.

2h: Light yellow powder, mp: 53–54°C. Anal. calc. for $C_{11}H_{12}BrN_3$: C, 49.64%; H, 4.54%; N, 15.79%; found: C, 49.75%; H, 4.50%; N, 15.86%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.23 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 6.97 (d, 1H, $J = 7.5$ Hz, Py), 7.49 (d, 1H, $J = 8.0$ Hz, Py), 7.58–7.63 (m, 1H, Py). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 12.64, 13.56, 24.24, 98.54, 112.70, 120.83, 138.70, 139.08, 148.24, 152.72, 157.08. IR (KBr): ν (cm^{-1}) 2981w, 2923m, 2852w, 1601s, 1582s, 1557m, 1484s, 1446vs, 1383s, 1361s, 1286w, 1270w, 1233w, 1180w, 1152w, 1098m, 1056s, 1015m, 880w, 790s, 762m, 730w, 681m, 657w, 606w.

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3h: White powder, mp: 58–59°C. Anal. calc. for $C_{11}H_{12}ClN_3$: C, 59.60%; H, 5.46%; N, 18.95%; found: C, 59.71%; H, 5.39%; N, 18.97%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.21 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 6.94 (d, 1H, $J = 7.5$ Hz, Py), 7.49 (d, 1H, $J = 8.0$ Hz, Py), 7.56–7.61 (m, 1H, Ph). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 11.60, 12.58, 24.15, 111.49, 112.38, 120.58, 137.26, 138.58, 146.66, 152.76, 156.91. IR (KBr): ν (cm^{-1}) 2984w, 2954w, 2924m, 2851w, 1600s, 1583s, 1486s, 1455vs, 1385s, 1365s, 1286w, 1234w, 1180w, 1152w, 1109m, 1060s, 1020m, 881w, 790s, 762m, 730w, 684m, 660w, 620w.

2i: White solid, mp: 60–61°C (lit.:[21] 48–49°C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.19 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 7.37–7.42 (m, 2H, Ph), 7.49–7.51 (m, 1H, Ph), 7.86–7.89 (m, 2H, Ph).

3i: White solid. mp: 54–55°C. Anal. calc. for $C_{12}H_{11}ClN_2O$: C, 61.42%; H, 4.72%; N, 11.94%; found: C, 61.18%; H, 4.73%; N, 12.01%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.19 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 7.37–7.42 (m, 2H, Ph), 7.48–7.53 (m, 1H, Ph), 7.88 (d, 2H, $J = 7.8$ Hz, Ph). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 11.87, 12.41, 114.94, 128.03, 131.48, 132.64, 132.80, 140.43, 149.61, 167.96. IR (KBr): ν (cm^{-1}) 3069w, 3032w, 2974w, 2931w, 1702vs, 1600m, 1583m, 1490s, 1449s, 1407s, 1378vs, 1343vs, 1276vs, 1206m, 1182m, 1135w, 1084s, 1103w, 1011m, 990s, 935s, 797m, 782m, 712s, 686vs, 624m.

2j: White powder, mp: 199–200°C (lit.:[22] 198°C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42–7.52 (m, 6H, Ph), 7.80–7.82 (m, 4H, Ph).

3j: White powder, mp: 191–193°C (lit.:[23] 203–204°C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.46 (m, 6H, Ph), 7.77–7.79 (m, 4H, Ph).

2k: Yellow crystals, mp: 104–105°C. Anal. calc. for $C_{21}H_{14}BrN_3O_2$: C, 60.02%; H, 3.36%; N, 10.00%; found: C, 60.28%; H, 3.38%; N, 10.02%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20–7.43 (m, 11H, Ph + C_6H_4), 7.83–7.90 (m, 3H, Ph + C_6H_4). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 95.10, 125.25, 127.82, 128.21, 128.45, 128.75, 128.80, 129.37, 129.43, 129.50, 130.12, 131.62, 133.19, 133.38, 143.39, 145.83, 151.17; IR (KBr): ν (cm^{-1}) 3064w, 3037w, 2924w, 2861w, 1064m, 1584w, 1530s, 1490m, 1449m, 1348s, 1308m, 1188w, 1159m, 1111m, 1068w, 1030w, 964m, 920m, 851w, 769s, 699s, 625w.

2l: White powder, mp: 178–180°C. Anal. calc. for $C_{11}H_{19}BrN_2$: C, 50.97%; H, 7.39%; N, 10.81%; found: C, 50.90%; H, 7.38%; N, 10.84%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43 (s, 18H, *t*-Bu). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 28.70, 32.75, 89.01, 153.43. IR (KBr): ν (cm^{-1}) 3269s, 3083w, 2962s, 2929m, 2871m, 1630w, 1549m, 1485m, 1462m, 1427w, 1386w, 1363m, 1272m, 1231m, 1209w, 1136m, 1048m, 986s, 934w, 760m, 665m, 547w.

3l: White powder, mp: 187–189°C. Anal. calc. for $C_{11}H_{19}ClN_2$: C, 61.53%; H, 8.92%; N, 13.05%; found: C, 61.93%; H, 9.03%; N, 12.68%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (s, 18H, *t*-Bu). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 28.61, 32.46, 104.53, 153.30. IR (KBr): ν (cm^{-1}) 3261s, 3096w, 2964s, 2926m, 2869m, 1631w, 1556m, 1486m, 1266m, 1431w, 1390w, 1364m, 1275m, 1233m, 1133m, 1070m, 989m, 935w, 764m, 662m, 554w.

5: Light red brown powder, mp: 116–117°C. Anal. calc. for $C_{11}H_{11}Br_2N_3$: C, 38.29%; H, 3.21%; N, 12.18%; found: C, 38.18%; H, 3.15%; N, 11.99%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.12 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 2.48 (b, 2H, NH_2), 6.69 (d, 1H, $J = 8.5$ Hz, C_6H_3), 7.13 (d, $J = 2.1$ Hz, Ph), 7.23–7.26 (dd, 1H, $J = 8.6$, 2.1 Hz, C_6H_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 11.01, 12.53, 95.70, 108.96, 118.08, 126.17, 130.23, 132.75, 139.12, 142.46, 148.57. IR (KBr): ν (cm^{-1}) 3430m, 3331m, 3052w, 2961w, 2923w, 1612m, 1585w, 1552w, 1502s, 1466m, 1422m, 1378w, 1292w, 1251w, 1159w, 1077m, 1034w, 898w, 849w, 812m, 690w, 634w, 599m.

6: Red powder, mp: 120–121°C. Anal. calc. for $C_{11}H_{10}Br_3N_3$: C, 31.17%; H, 2.38%; N, 9.91%; found: C, 31.07%; H, 2.39%; N, 9.80%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.11 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 7.10 (d, $J = 2.1$ Hz, C_6H_2), 7.55 (d, $J = 2.1$ Hz, C_6H_4). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 11.13, 12.61, 96.18, 108.19, 110.74, 126.10, 129.61, 135.24, 139.28, 141.08, 149.14. IR (KBr): ν (cm^{-1}) 3408m, 3281m, 3217m, 3178m, 3077w, 2955w, 2920w, 2853w, 1624s, 1558m, 1464vs, 1429m, 1376w, 1352w, 1302w, 1271w, 1226w, 1077s, 1047m, 9878w, 895w, 863m, 807w, 721m, 658m, 632m, 606w, 551m.

9: Red solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.11 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 6.93 (d, $J = 2.1$ Hz, C_6H_2), 7.27 (d, $J = 2.1$ Hz, C_6H_2).

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