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Halogenations of 3-aryl-1*H*-pyrazol-5-amines

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Abstract

A direct C-H halogenation of 3-aryl-1*H*-pyrazol-5-amines with NXS (X = Br, I, Cl) as cheap and safe halogenating reagents at room temperature has been developed. This transformation provides an effective metal-free protocol towards the synthesis of novel 4-halogenated pyrazole derivatives with moderate to excellent yields. The method represents simple and mild reaction conditions, broad substrate scope as well as gram-scale synthesis. The utility of this procedure is established by further transformations of the 4-halogenated products. Mechanism studies show that DMSO plays a dual role of catalyst and solvent.

Keywords

Halogenation; Metal-free; Pyrazol-5-amine; Synthesis; 4-halogenopyrazole

Introduction

Pyrazole is one of the most popular heterocycles in bioactive compounds, including drugs and agrochemicals [1, 2]. Among them, halogenated pyrazoles have shown

significant utilization in various transition-metal-catalyzed C-R (R = C, N, etc.) coupling reactions [3]. It has also been used as an important synthon in the synthesis of pharmaceutically privileged bio-heterocycles, the skeletal core of medicines, and pesticides. For example, many 3/5-halogenopyrazoles have been reported for their use in crop sciences (**Figure 1**) [4, 5], such as activator of insect's ryanodine calcium channel receptors (Ryraxypyr **1**) [6−9], herbicide (Halosulfuron methy **2**) [10], and inhibitors of complex II succinate dehydrogenase (Penfiufen **3** and Furamethpy **4**) [11, 12]. In addition, the halogenopyrazoles with potential medical have been used in various pathologies **Figure 1**), such as inhibitor of the serine/threonine protein kinase Akt (**5**) [13], inhibitor of tubulin polymerization (**6**) [14], antagonists of P2X 7 receptors (**7**) [15], and positive allosteric modulator of metabotropic glutamate receptor mGluR4 (**8**) [16]. The most common strategy to construct halogenated pyrazole skeletons involves: (i) electrophilic halogenation of pyrazoles or pyrazole anions; (ii) dehydroxyhalogenations of 3/5-hydroxypyrazoles; (iii) halogenodediazoniations of 3/5-aminopyrazoles; (iv) rearrangements as well as cycloaddition or condensation reactions involving halogen-bearing substrates; (v) modifications of 3,5-halogenopyrazoles (i.e., halogen exchanges, alkylation, oxidation, etc.) [3a,17]. However, some problems such as the use of toxic halogen sources, poor regioselectivity, harsh reaction conditions, and narrow substrate ranges remain as challenges for these methods. Recently, the direct C–H halogenation of arene has gained considerable attention in the synthesis of organohalides. In this context, significant advances have been made in the direct halogenation catalyzed by transition metals or metal-free Conditions [18, 19]. But to the best of our knowledge, the direct halogenation of pyrazol-5-amine is rare in the literature. In particular, the direct halogenation of N-arylsulfonyl-5-aminopyrazole has never been reported. In 2014, Tu group reported an oxidative dehydrogenative couplings of pyrazol-5-amines in the

presence of iodine and TBHP, the reaction simultaneously installs C−I and N−N bonds through iodination and oxidation (**Scheme 1a**) [20]. As part of our interest in the direct C-H functionalization of heterocycles [21], we herein reported a direct C-H halogenation of 3-aryl-1*H*-pyrazol-5-amines for the synthesis of novel 4-halogenopyrazoles derivatives (**Scheme 1b**).

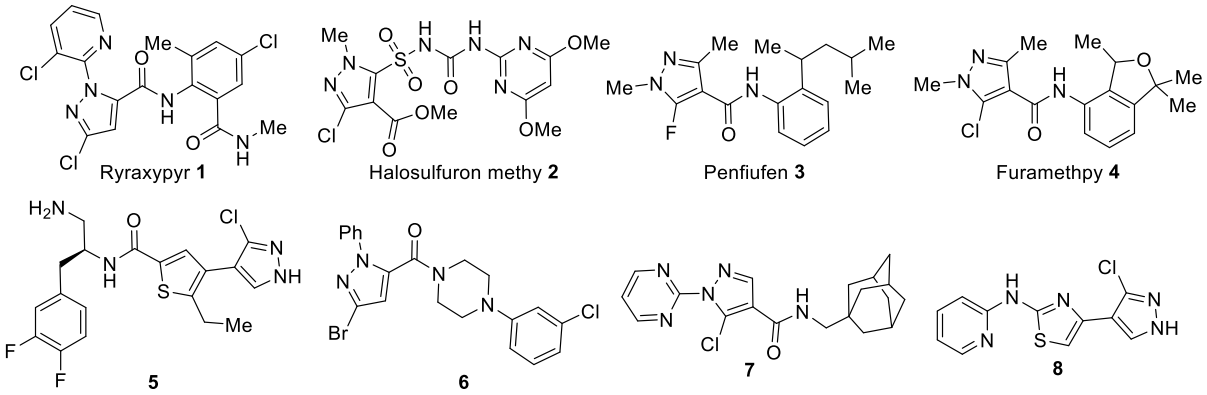
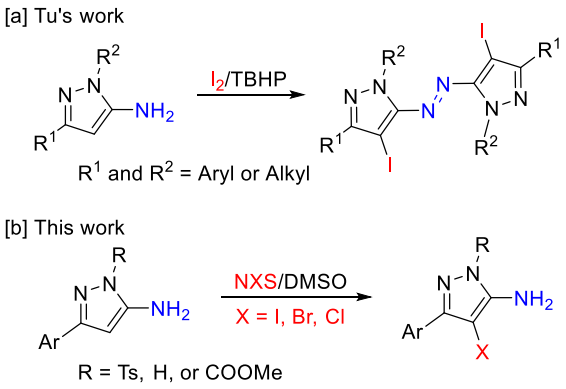


Figure 1: Representative biologically active compounds with halogenopyrazole motif.



Scheme 1: Halogenation of pyrazol-5-amine derivatives.

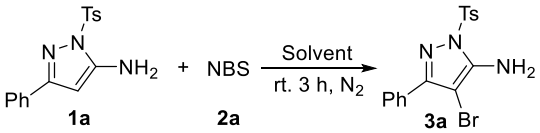
Results and Discussion

Optimization of the reaction conditions

Initially, we chose 0.2 mmol of 3-phenyl-1-tosyl-1*H*-pyrazol-5-amine (**1a**) and 0.3 mmol of NBS (**2a**) as reactants to investigate the feasibility of this reaction (**Table 1**). First, this reaction was performed in *n*-hexane at room temperature for 3 hthe C-4

bromination product (**3a**) was successfully obtained with a yield of 65% (entry 1). Subsequently, we examined the effects of other solvents on the reaction (entries 2-8). The results showed that when ethanol and 1,4-dioxane were used as solvents, low yields were obtained (entries 2 and 3). In contrast, DCM, EtOAc, MeCN, and DMF are selected as solvents to provide relatively good yields (70-82%, entries 4-7). To our delight, DMSO as a solvent gave an excellent yield (95%, entry 8). Next, we adjusted the amount of NBS to 1.2 equiv, the reaction also proceeded smoothly to furnish the product 3a in nearly equivalent yield (99%, entry 9). Shortening the reaction time led to a decrease in yield (entry 10). Finally, the optimal reaction conditions emerged as **1a** (0.2 mmol), **2a** (1.2 equiv.), and DMSO (2 mL) at room temperature for 3 h under N_2 atmosphere (entry 9).

Table 1. Optimized reaction conditions[a].



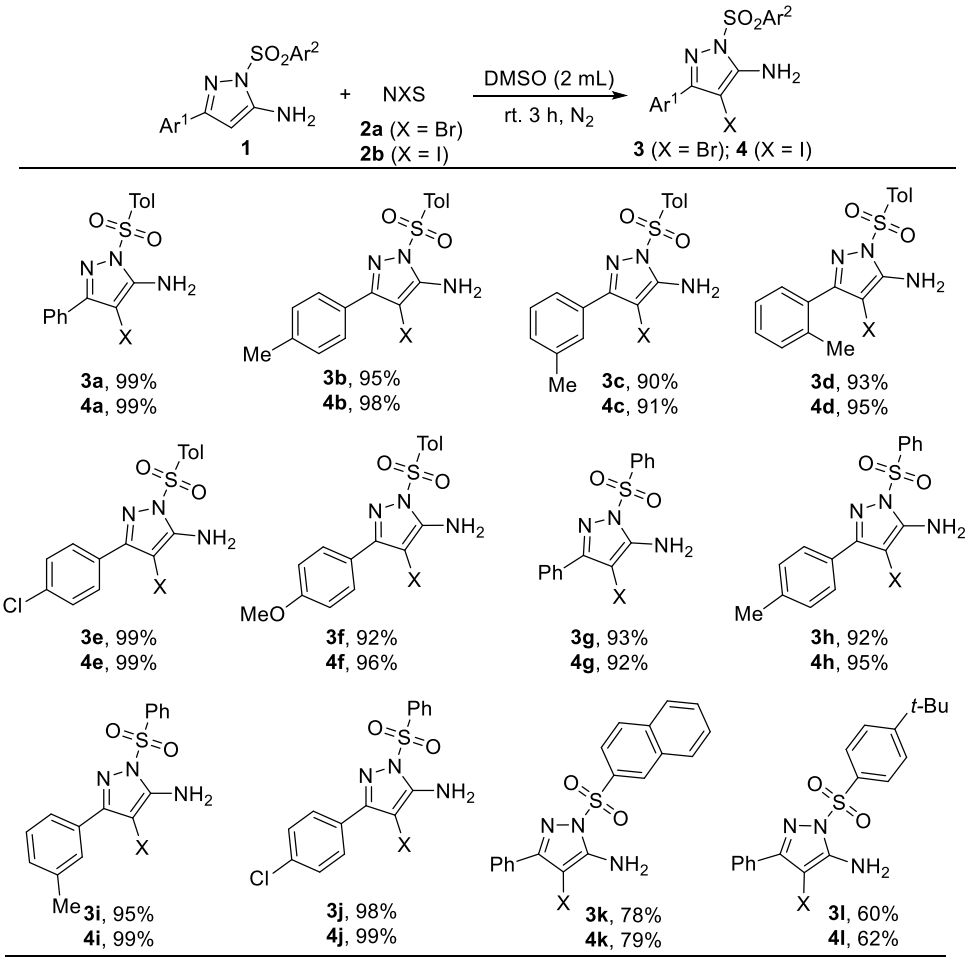
Entry	**1a/2a**	Solvent	t(h)	Yield(%)[b]
1	1:1.5	*n*-hexane	3	65
2	1:1.5	EtOH	3	31
3	1:1.5	1,4-dioxane	3	55
4	1:1.5	DCM	3	75
5	1:1.5	EtOAc	3	79
6	1:1.5	CH_3CN	3	70
7	1:1.5	DMF	3	82
8	1:1.5	DMSO	3	95
9	**1:1.2**	**DMSO**	**3**	**99**

10	1:1.2	DMSO	2	87

[a]Reaction conditions: **1a** (0.2 mmol), NBS (**2a**), solvent (2 mL), room temperature, under N_2 atmosphere; [b] Isolated yields.

Next, With the optimized reaction conditions in hand, we then investigated the scope of *N*-arylsulfonyl-3-aryl-5-aminopyrazole with NBS/NIS (**Table 2**). The results showed that the substituents on the aromatic ring of 3-aryl-1-tosyl-1*H*-pyrazol-5-amines did not hamper the reaction process. Reactions of methyl-, chloro-, or methoxy-substituted substrates with NBS proceeded efficiently to afford the desired products **3b-3f** in excellent yields. The reactions were successful for both electron-donating and electron-withdrawing substituents on the aromatic rings. When 3-aryl-1-phenylsulfonyl-1*H*-pyrazol-5-amines were used as reactants, the brominated reaction still occurred smoothly to deliver the brominated products **3g-3j** with excellent yields. The results indicated that the type and position of the substituents on the aromatic ring of the substrate had no obvious influence on the reactivity. To our delight, the structure of **3j** was determined by single crystal X-ray diffraction (**Figure 2**, CCDC: 2090203). In addition, variation of nitrogen-tethered substituents on the pyrazole ring including naphthalen-2-ylsulfonyl and (4-(*tert*-butyl)phenyl)sulfonyl groups were tolerated well, leading to the desired products **3k** and **3l** in 78% and 60% yields, respectively. Similarly, the iodination of *N*-arylsulfonyl-3-aryl-5-aminopyrazole with NIS succeeded in obtaining the corresponding iodinated product **4a-4l** with moderate to excellent yields.

Table 2. Reactions of *N*-arylsulfonyl-3-aryl-5-aminopyrazoles with NBS/NIS. [a]



[a]Reaction condition: **1** (0.20 mmol), **2** (0.24 mmol), DMSO (2 mL), room temperature, 3 h, under N_2 atmosphere; Isolated yield

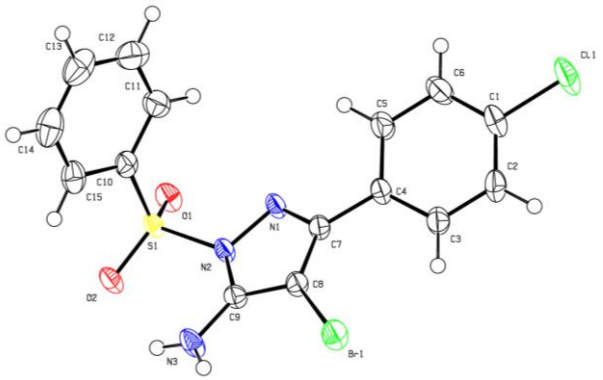
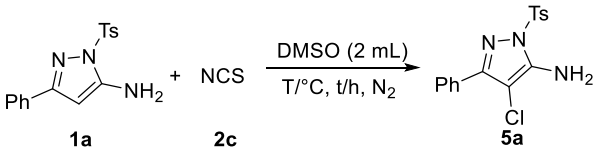


Figure 2: The crystal structure of **3j**. (CCDC: 2090203)

Based on the above reactions, we then turned our attention toward examining the chlorination of *N*-arylsulfonyl-3-aryl-5-aminopyrazole (**Table 3**). First, the reaction of 3-phenyl-1-tosyl-1*H*-pyrazol-5-amine (**1a**, 0.2 mmol) and NCS (**2c**, 0.3 mmol) was

performed at room temperature for 3 h, but only 55% yield of the chlorinated product **5a** was obtained (entry 1). Increasing the temperature was detrimental to the reaction (entry 2). Further studies indicated that the efficiency of this transformation was improved when 2.5 equiv. of **2c** was used (68%, entry 3). However, continuing to increase the amount of **2c** or extending the reaction time has no significant effect on the yield of the chlorination (entries 4 and 5).

Table 3. Optimization of reaction conditions for **1a** and NCS[a].



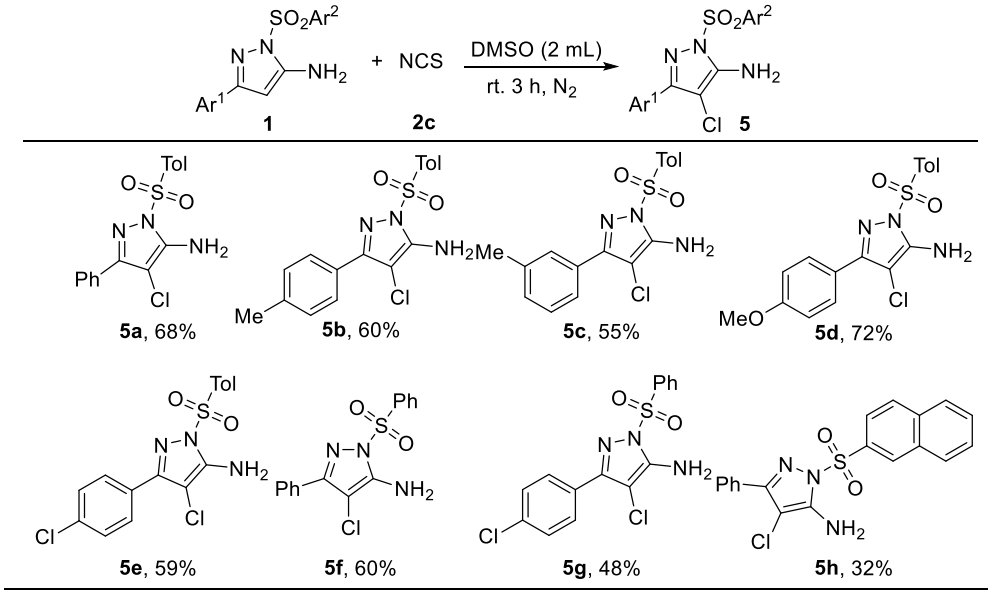
Entry	**1a**/**2c**	T(°C)	t(h)	Yield(%)[b]
1	1:1.5	rt	3	55
2	1:1.5	50	3	50
3	1:2.5	rt	3	68
4	1:2.5	rt	6	68
5	1:3.5	rt	3	69

[a] Reaction conditions: **1a** (0.2 mmol), DMSO (2 mL), under N_2 atmosphere; Isolated yield.

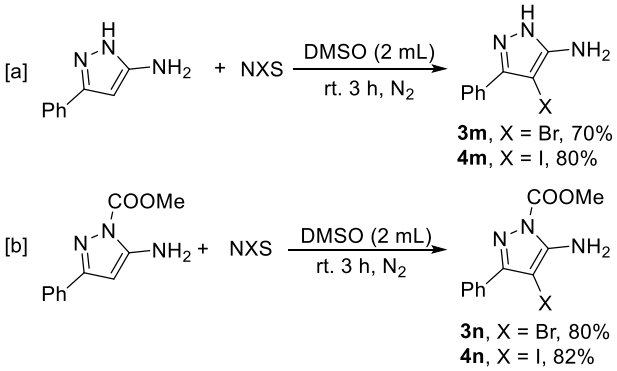
Next, we expanded the scope of this chlorination of *N*-arylsulfonyl-3-aryl-5-aminopyrazole with NCS (**Table 4**). Various 3-aryl-1-tosyl-1*H*-pyrazol-5-amines could be successfully transformed into the target products **5b-5e** in 55-72% yields. The chlorinations of 3-aryl-1-(phenylsulfonyl)-1*H*-pyrazol-5-amines were successful, affording the desired products **5f** and **5g** in 60% and 48% yields, respectively. Unfortunately, 1-(naphthalen-2-ylsulfonyl)-3-phenyl-1H-pyrazol-5-amine was used as a reactant, the desired product **5h** was obtained in 32% yield.

Gratifyingly, the halogenation reactions were compatible with the substrate 3-phenyl-1*H*-pyrazol-5-amine, generating the product **3m** and **4m** in 70% and 80% yields, respectively (**Scheme 2[a]**). In addition, the ester group (1-COOMe) on the pyrazoles of the substrate were also well-tolerated, the desired products **3n** and **4n** in good yields (**Scheme 2[b]**). The structure of **4n** was determined by single crystal X-ray diffraction (**Figure 3**, CCDC: 2090220).

Table 4. Reactions of *N*-arylsulfonyl-3-aryl-5-aminopyrazoles with NCS[a].



[a]Reaction condition: **1** (0.20 mmol), **2c** (0.5 mmol), DMSO (2 mL), room temperature, 3 h, under N_2 atmosphere; Isolated yields.



Scheme 2: The reactions of 3-phenyl-1*H*-pyrazol-5-amine derivatives with NXS (X = Br, I).

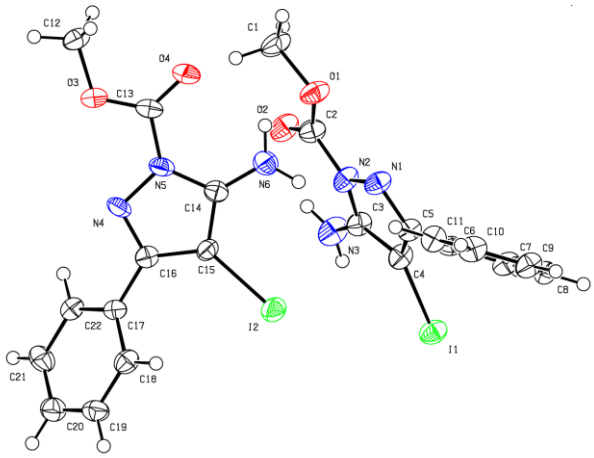
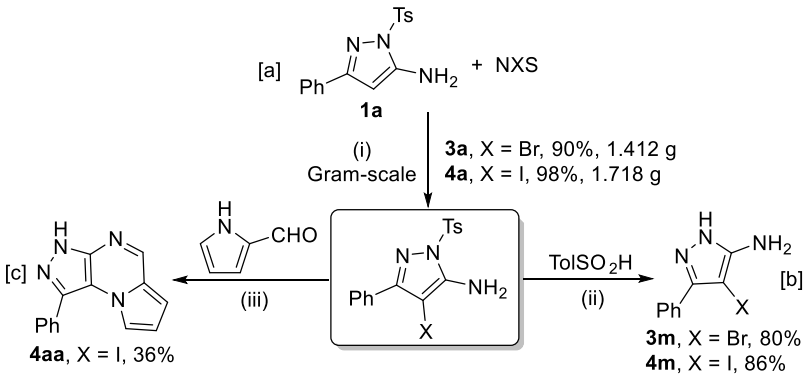


Figure 3: The crystal structure of **4n** (CCDC: 2090220).

To demonstrate the usefulness of the halogenation reaction, we conducted two gram-scale reactions of **1a** with NBS and NIS. The gram-level products **3a** (1.412 g) and **4a** (1.718 g) could be isolated with excellent yields (**Scheme 3[a]**). Furthermore, the products **3a** and **4a** could successfully remove the Ts group under the action of *p*-toluenesulfinic acid ($TolSO_2H$), the products **3m** and **4m** were obtained in 80% and 86% yields, respectively (**Scheme 3[b]**). In the presence of 3 equivalents of Cs_2CO_3 (0.6 mmol), **4a** (0.2 mmol) reacted with 1*H*-pyrrole-2-carbaldehyde (0.2 mmol) in DMF (1 mL) at 120 °C for 12 h to afford the cyclized product 1-phenyl-3*H*-pyrazolo[3,4-*e*]pyrrolo[1,2-*a*]pyrazine **4aa** in 36% yield (**Scheme 3[c]**).

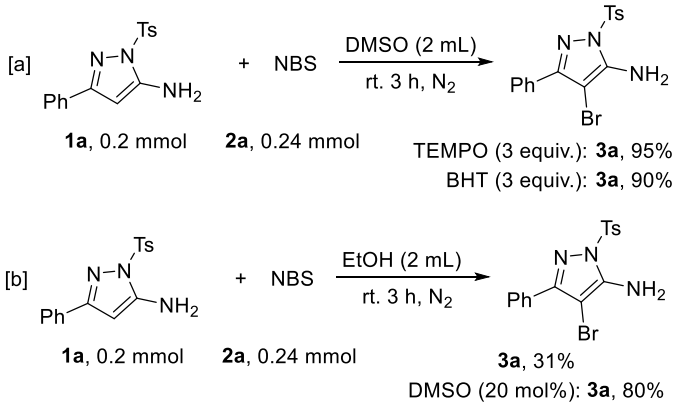


Reaction conditions: (i) **1a** (4.0 mmol), NXS (X = Br or I, 4.8 mmol), DMSO (10 mL), room temperature, 6 h, N_2. (ii) **3a** or **4a** (0.2 mmol), $TolSO_2H$ (0.4 mmol), EtOH (0.5

mL), 80 °C, 12 h; (iii) **4a** (0.2 mmol), 1*H*-pyrrole-2-carbaldehyde (0.2 mmol), Cs_2CO_3 (0.6 mmol), DMF (1 mL), 120 °C, 12 h.

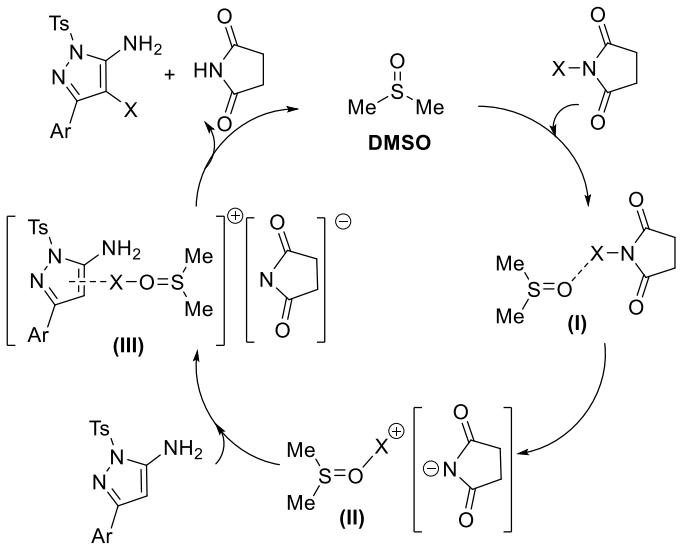
Scheme 3: Gram-scale synthesis and derivatization of **3a** and **4a.**

To gain the reaction mechanism, we performed a series of control experiments (**Scheme 4**). In the presence of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) or BHT (2,6-ditertbutyl-4-methylphenol), the halogenation of **1a** with **2a** was not suppressed, and the product **3a** was obtained in 95% and 90% yields, respectively (**Scheme 4[a]**). The result shows that a free radical pathway is not involved in the transformation process. In addition, we found that this reaction only gave a yield of 31% when ethanol was used as the solvent. However, with the addition of 20 mol% DMSO, the bromination yield can be increased to 80%. This result indicates that DMSO should play a dual role as catalyst and solvent in the halogenation process.



Scheme 4: Control experiments.

On the basis of our experimental results and previous reports,[19a] a plausible halogenation mechanism is proposed (**Scheme 5**). Initially, the oxygen atom of DMSO coordinated with the halogen atom of NXS to form the polarized intermediate DMSO·X^+ (I). [22-25] Subsequently, DMSO·X^+ (II) reacts with π electrons of 5-aminopyrazole to form the intermediate (III). Finally, the halogenated product is obtained with the formation of succinimide and DMSO for the next catalytic circle.



Scheme 5: The plausible mechanism.

Conclusion

In summary, we have realized the direct C-H halogenation of 3-aryl-1*H*-pyrazol-5-amines and NXS (X = Br, I, Cl) at room temperature. This protocol provides efficient access to various 4-halogenated pyrazole derivatives with moderate to excellent yields as well as broad substrate scope. The results of the control experiments show that DMSO plays a dual role of catalyst and solvent in the halogenation process. The characteristics of simple and mild reaction conditions, low-cost and ease of handling NXS as halogenating reagent, reliable scalability, and flexibility of structural modification make this method a useful tool for the building of widely diversified pyrazoles with potential value in the fields of medicine and synthesis.

Experimental

Materials and instruments

Unless otherwise noted, all synthetic steps were performed under the air atmosphere using sealed tube. The materials obtained from commercial sources were used without

further purification. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on a Brucker Advance III HD 400 MHz spectrometer in $CDCl_3$ solution. All chemical shifts were reported in ppm (δ) relative to the internal standard TMS (0 ppm). High-resolution mass spectra (HRMS) were acquired in electrospray ionization (APCI) mode using a TOF mass analyzer.

General procedure for N-arylsulfonyl-3-aryl-5-aminopyrazole with NBS or NIS.

A mixture of *N*-arylsulfonyl-3-aryl-5-aminopyrazole (**1**, 0.2 mmol), NIS or NBS (0.24 mmol), and DMSO (2 mL) was stirred at room temperature for 3 hours under N_2 atmosphere. Upon completion, the reaction was quenched with 5 ml of sodium thiosulfate solution and extracted with dichloromethane (5 mL × 3), saturated with NaCl solution (5 mL × 3), and concentrated *in vacuo*. The crude residue was purified by flash chromatography (DCM/EtOH) to afford the desired products **3** or **4**.

General procedure for N-arylsulfonyl-3-aryl-5-aminopyrazole with NCS.

A mixture of *N*-arylsulfonyl-3-aryl-5-aminopyrazole (**1**, 0.2 mmol), NCS (0.5 mmol), and DMSO (2 mL) was stirred at room temperature for 3 hours under N_2 atmosphere. Upon completion, the reaction was extracted with dichloromethane (5 mL × 3), saturated with NaCl solution (5 mL × 3), and concentrated *in vacuo*. The crude residue was purified by flash chromatography (DCM/EtOH) to afford the desired product **5**.

General procedure for gram-scale synthesis of 3a or 4a.

A mixture of 3-phenyl-1-tosyl-1*H*-pyrazol-5-amine (**1a**, 4.0 mmol), NIS or NBS (4.8 mmol), and DMSO (10 mL) was stirred at room temperature for 6 h under N_2 atmosphere. Upon completion, the reaction was quenched with 25 ml of sodium thiosulfate solution and extracted with dichloromethane (25 mL × 3), saturated with NaCl solution (25 mL × 3), and concentrated *in vacuo*. The crude product is recrystallized in ethanol. In addition, the small amount of product **3a** remaining in the

ethanol filtrate could be further separated by silica gel column chromatography (DCM/EtOH). Finally, 1.412 g of the product **3a** and 1.718 g of the product **4a** were obtained with 90% and 98% yields, respectively.

Typical procedure for the synthesis of 3m and 4m

A mixture of 4-bromo-3-phenyl-1-tosyl-1*H*-pyrazol-5-amine (**3a**, 0.2 mmol), $TolSO_2H$ (2 equiv.), and ethanol (0.5 mL) was stirred at 80 ^oC for 12 h. Upon completion, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (PE/EtOAc) to afford the final products **3m** and **4m**.

Typical procedure for the synthesis of 4aa

AA mixture of 4-iodo-3-phenyl-1-tosyl-1*H*-pyrazol-5-amine (4a, 0.2 mmol), 1*H*-pyrrole-2-carbaldehyde (0.2 mmol), Cs_2CO_3 (0.6 mmol), and DMF (1 mL) was stirred at 120 ^oC for 12 h under N_2 atmosphere. Upon completion, the solution was added with 5 ml of saturated NaCl solution and extracted with EtOAc. The organic solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (PE/EtOAc) to afford the final product **4aa**.

Supporting Information

Supporting Information File 1: Characterization data and ^1H NMR, ^{13}C NMR spectra of the synthesized compounds.

Acknowledgements

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References

1. Taylor, R. D.; MacCoss, M.; Lawson, A. D. G. *J. Med. Chem.,* **2014**, *57* 5845–5859.
2. MacBean, C. *The Pesticide Manual, British Crop Production Council.* **2012**.
3. (a) Janin, Y. L. *Chem. Rev.*, **2012**, *112*, 3924–3958; (b) Jedinák, L.; Cankař, P. *Eur. J. Org. Chem.,* **2016**, *11*, 2013–2023; (c) Jedinák, L.; Zátopková, R.; Zemánková, H.; Šustková, A.; Cankař, P. *J. Org. Chem.,* **2017**, *82*, 157–169; (d) Fu, L.; Xu, Z.; Wan, J. P.; Liu, Y. *Org. Lett.,* **2020**, *22*, 9518–9523; (e) Pan, Y.; Gong, Y.; Song, Y.; Tong, W.; Gong, H. *Org. Biomol. Chem.* **2019**, *17*, 4230–4233; (f) Xiong, J.; Zhong, G.; Liu, Y. *Adv. Synth. Catal.,* **2019**, *361,* 550–555.
4. Lamberth, C. *Heterocycles,* **2007**, *71,* 1467–1502.
5. Krämer, W.; Schirmer, U.; Jeschke, P.; Witschel, M.; *Modern methods in crop protection Research.* **2012**, *2012*, 273–305.
6. Lahm, G. P.; Selby, T. P.; Freudenberger, J. H.; Stevenson, T. M.; Myers, B. J.; Seburyamo, G.; Smith, B. K.; Flexner, L.; Clark, C. E.; Cordova, D. *Bioorg. Med. Chem. Lett.,* **2005**, 15, 4898–4906.
7. Lahm, G. P.; Stevenson, T. M.; Selby, T. P.; Freudenberger, J. H.; Cordova, D.; Flexner, L.; Bellin, C. A.; Dubas, C. M.; Smith, B. K.; Hughes, K. A.; Hollingshaus, J. G.; Clark, C. E.; Benner, E. A. *Bioorg. Med. Chem. Lett.,* **2007**, *17*, 6274–6279.
8. Clark, D. A.; Lahm, G. P.; Smith, B. K.; Barry, J. D.; Clagg, D. G. *Bioorg. Med. Chem.,* **2008**, *16,* 3163–3170.
9. Lahm, G. P.; Cordova, D.; Barry, J. D.; *Bioorg. Med. Chem.*, **2009,** *17*, 4127–4133.
10. Gregory, V.; Pasteris, R. J. Patent WO 2009055514, **2009**.
11. Morimoto, K.; Sato, T.; Yamamoto, S.; Takeuchi, H. *J. Heterocycl. Chem.*, **1997**, *34*, 537–540.

12. Dunkel, R.; Elbe, H. L.; Greul, J. N.; Hartmann, B.; Gayer, H.; Seitz, T.; Wachendorff–Neumann, U.; Dahmen, P.; K. Kuck, H. Patent WO 2006061215, **2006**.
13. Paruch, K.; Guzi, T. J.; Dwyer, M. P. Patent WO 09070567, **2009**.
14. Rouse, M.; Seefeld, M. A.; Patent WO 2010093885, **2010**.
15. Li, H.; Yuan, J.; Bakthavatchalam, R.; Hodgetts, K.J.; apitosti, S. M.; Mao, C. J.; Wustrow, D. J.; Guo, Q. Patent WO 2009012482, **2009**.
16. Bolea, C. Patent WO 10079239, **2010**.
17. (a) Zhao, Z. G.; Wang, Z. X. *Synth. Commun.,* **2007**, *37,* 137–147; (b) Fu, L.; Bao, X.; Li, S.; Wang, L.; Liu, Z.; Chen, W.; Xia, Q.; Liang, G.; *Tetrahedron*, **2017**, *73,* 2504–2511.
18. (a) Mykhailiuk, P. K. *Chem. Rev.,* **2021**, *121,* 1670–1715; (b) Luo, J. F.; Xu, X.; Zhao, Y. C.; Liang, H. Z. *Chin. J. Org. Chem.,* **2017**, *37,* 2873–2882; (c) Zeng, Z. G.; Sang, X. K.; Yuan, B.; Wu, M. H.; Zhang, Y. W. *Chin. J. Org. Chem.,* **2021**, *41* ,959–968; (d) Petrone, D. A.; Ye, J.; Lautens, M. *Chem. Rev.*, **2016**, *116,* 8003–8104; (e) Liu, D.; Zhu, Y. Y.; Gu, S. X.; Chen, F. E. *Chin. J. Org. Chem.*, **2021**,*41,*1002–1011; (f) Liao, G.; Shi, B. F. *Acta Chim. Sinica.*, **2015**, 73, 1283–1293; (g) Tang, R. J.; Milcent, T.; Crousse, B. *J. Org. Chem.,* **2018**, *83,* 930–938; (h) Udavant, R. N.; Yadav, A. R.; Shinde, S. S. *Eur. J. Org. Chem*., *2018*, *26,* 3432–3436, (i) Stefani, H. A.; Pereira, C. M. P.; Almeida, R. B.; Braga, R. C.; Guzen, K. P.; Cella, R. *Tetrahedron lett.,* **2005**, *46,* 6833–6837; (j) Olsen, K. L.; Jensen, M. R.; MacKay, J. A.; Tetrahedron lett.; *2017*, *58*, 4111–4114.
19. (a) Song, S.; Li, X.; Wei, J.; Jiao, N. *Nat. Catal,* **2020**, *3*, 107–115; (b) Fosu, S. C. C.; Hambira, M.; Chen, A. D.; Fuchs, J. R.; Nagib, D. A. *Chem.,* **2018**, *5,* 417–428; (c) Tanemura, K.; Suzuki, T.; Nishida, Y.; Satsumabayashi, K.; Horaguchi, T. *Chem. Lett.,* **2003**, *32*, 932–933; (d) Xiong, X.; Yeung, Y. Y. *ACS Catal.,* **2018**, *8,*

4033–4043; (e) Wang, M.; Zhang, Y.; Wang, T.; Wang, C.; Xue, D.; Xiao, J. *Org. Lett.,* **2016**, *18,* 1976–1979; (f) Maddox, S. M.; Nalbandian, C. J. Smith, D. E.; Gustafson, J. L. *Org. Lett.,* **2015**, *17,*1042–1045; (g) Zhang, L.; Hu, X. *Chem. Sci.*, **2017**, *8,* 7009–7013; (h) Rodriguez, R. A.; C. Pan, M.; Yabe, Y.; Kawamata, Y.; Eastgate, M. D.; Baran, P. S. *J. Am. Chem. Soc.,* **2014**, *136,* 6908–6911; (i) Luo, T.; Tian,S. H.; Wan, J.; Liu, Y. Y. *Curr. Org. Chem.*, **2021**, *25,* 1180–1193; (j) Lin, Y.; Wan, J. P.; Liu, Y. *New J. Chem.,* **2020**, *44*, 8120–8124; (k) Li, Z. H.; Fiser, B.; Jiang, B. L.; Li, J. W.; Xu, B. H.; Zhang, S. J. *Org. Biomol. Chem.,* **2019**, *17*, 3403–3408; (l) Ma, X.T.; Zhou, K. J.; Ren, M. J.; Wang, M. Y.; Yu, J. *Chin. J. Org. Chem.,* **2019**, *39,* 2796–2801.

20. Jiang, B.; Ning, Y.; Fan, W.; Tu, S. J.; Li, G. *J. Org. Chem.,* **2014**, *79,* 4018–4024.
21. (a) Wei, Y.; Liu, P.; Liu, Y.; He, J.; Li, X.; Li, S.; Zhao, J. *Org. Biomol. Chem.,* **2021**, *19,* 3932–3939; (b) Yang, Z.; He, J.; Wei, Y.; Li, W.; Liu, P.; Zhao, J.; Wei, Y. *Org. Biomol. Chem*., **2020**, *18,* 9088–9094; (c) Yang, Z.; He, J.; Wei, Y.; Li, W.; Liu, P. *Org. Biomol. Chem.,* **2020**, *18,* 3360–3366; (d) Liu, Y.; Wei, Y.; Yang, Z.; Li, Y.; Liu, Y.; Liu, P. *Org. Biomol. Chem.,* **2021**, *19,* 5191–5196; (e) Wei, Y. T.; Liu, Y. L.; He, J.; Li. X. Z.; Liu, P.; Zhang, J. *Tetrahedron*, 2020, *76*, 131646–131646; (f) Wei, Y.; He, J.; Liu, Y.; Xu, L.; Vaccaro, L.; Liu, P.; Gu, Y. *ACS Omega*., **2020**, *5,* 18515–18526; (g) Chen, L.; Zhang, J.; Wei, Y.; Yang, Z.; Liu, P.; Zhang, J.; Dai, B. *Tetrahedron*, **2019**, *75*, 130664–130664; (h) Zhang, J.; Wang, Z.; Chen, L.; Liu, Y.; Liu, P.; Dai, B. *RSC Adv.,* **2018**, *8,* 41651–41656; (i) Chen, L.; Liu, P.; Wu, J.; Dai, B. *Tetrahedron*, **2018**, *74*, 1513–1519; (j) Li, Y.; Yang, Z.; Liu, Y.; Liu, Y.; Gu, Y.; Liu, P. *Mol. Catal.,* **2021**, *511*, 111747–111754.
22. Cresswell, A. J.; Eey, T. C. S.; Denmark, S. E. *Nat. Chem.,* **2015**, *7*, 146–152.
23. Samanta, R. C.; Yamamoto, H. *J. Am. Chem. Soc.,* **2017**, *139*, 14605–14610.
24. Sakakura, A.; Ukai, A.; Ishihara, K. *Nature*, **2007**, *445,* 900–903.

25. Seidl, F. J.; Min, C.; Lopez, J. A.; Burns, N. Z.; *J. Am. Chem. Soc.,* **2018**, *140*, 15646–1550.