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A novel one-pot approach to oxidative aromatization and bromination of pyrazolidin-3-one with HBr-H_2O_2 system

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Abstract: An efficient and green one-pot method for the oxidative aromatization and bromination of pyrazolidin-3-ones under mild conditions with a HBr-H_2O_2 system was developed. A mechanism was proposed.

Keywords: aromatization; bromination; bromopyrazol; hydrogen bromide; hydrogen peroxide; one-pot; oxidative; pyrazolidin-3-one.

Introduction

Pyrazole derivatives attract attention due to their excellent pharmacological properties [1–4]. Halogenated pyrazolols [5, 6], especially 4-bromo derivatives, are precursors for the synthesis of functionalized pyrazoles [7–9], such as pharmaceuticals [10], multifunctional materials [11, 12], fused- [13] and spiro-heterocyclic compounds [14]. Various protocols for the synthesis of brominated pyrazolols have been reported. However, bromination of pyrazolols with Br_2 in acetic acid is carried out under harsh conditions and requires careful manipulation [15]. Efforts have been made by Ahmed et al. [16] to use the photolysis of *N*-bromosuccinimide as the source of bromine [16]. Due to the formation of the coupling by-products, bromopyrazolols are afforded in low yields. Although *N*-bromobenzamide [17] and dibromoisocyanuric acid [18] have also been explored as mild brominating agents for pyrazolols, these approaches have met with limited success.

Recently, pyrazolidinones have been reported as substrates for the synthesis of pyrazolols [7, 11, 12, 19–23]. Unfortunately, few efficient methods for direct access to 4-bromopyrazolol from pyrazolidinone have been reported. Traditionally, there are two steps in the synthesis of 4-bromopyrazolol from pyrazolidinone [7, 11, 12] that involve aromatization of pyrazolidin-3-ones to give pyrazol-3-ols and bromination of pyrazol-3-ols [7]. This protocol requires the use of a transition-metal catalyst, extremely toxic liquid bromine, a long reaction time, multi-step manipulations and the final yield is only moderate. In recent years, brominations with safe bromination reagents and green co-oxidants have received growing attention because of their greenness and high efficiency [24]. Herein, we report a novel one-pot, metal-free, atom-economic and highly effective method for the preparation of 4-bromopyrazol-3-ol from pyrazolidin-3-one using a HBr-H_2O_2 system under mild conditions.

Results and discussion

The starting compounds **1** (Scheme 1) were commercially available or easily prepared according to previously published procedures [7, 11, 12, 19–23]. Initially, 1-(4-chlorophenyl)-pyrazolidin-3-one (**1a**) was treated with various amounts of hydrogen peroxide and hydrobromic acid using various solvents. It was found that the use of different solvents including carbon tetrachloride, chloroform, dichloromethane, methanol and *N,N*-dimethylformamide had little effect on the outcome, affording the yield of the product **2a** in the range from 72% to 90%. Nevertheless, the highest yield of 90% was obtained for the reaction conducted in chloroform. Under optimized conditions, the synthesis of **2a** was conducted in chloroform at 60°C using 3 equivalents of H_2O_2 and 1 equivalent of HBr.

Decreasing the amount of hydrogen peroxide to 1 equivalent or 2 equivalents resulted in a decrease of the yield of the product **2a**. On the other hand, an increase in the amount of hydrogen peroxide from 3 equivalents to 4 equivalents did not affect the yield. With the optimized reaction conditions for **2a**, a wide range of 4-bromo-3-hydroxypyrazolidines were synthesized (Scheme 1). The reaction proceeds well with pyrazolidin-3-ones containing a phenyl group, a substituted phenyl group or a pyridinyl

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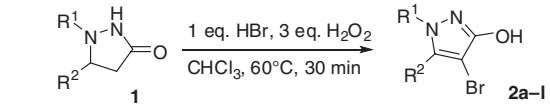


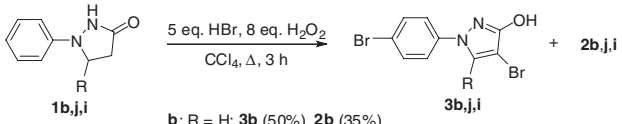
2a: R^1 = 4-Cl-C_6H_4, R^2 = H
2b: R^1 = Ph, R^2 = H
2c: R^1 = 4-F-C_6H_4, R^2 = H
2d: R^1 = 4-Me-C_6H_4, R^2 = H
2e: R^1 = 3-Cl-pyridin-2-yl, R^2 = H
2f: R^1 = 4-Cl-C_6H_4, R^2 = Me
2g: R^1=4-Cl-C_6H_4, R^2 = Ph
2h: R^1 = 4-Cl-C_6H_4, R^2 = MeO
2i: R^1 = Ph, R^2 = Ph
2j: R^1 = Ph, R^2 = Me
2k: R^1= 4-Me-C_6H_4, R^2 = Me
2l: R^1 = H, R^2 = Me

Scheme 1

group. With an increase in the electron-donating capability of the substituent at the 5-position of pyrazolidin-3-ones (MeO > CH_3 > H), the efficiency of the reaction is increased in the same order.

Interestingly, when the reaction with 5 equivalents of HBr was carried out for 3 h (Scheme 2), the corresponding dibrominated products **3b,j** were obtained accompanied by the corresponding monobrominated products **2b,j** in moderate yields. However, in the case of compound **1i** only monobrominated product **2i** was acquired in high yield. For further confirmation of the structure of the series, a single crystal of **3j** was obtained and subjected to X-ray diffraction analysis (Figure 1).

To gain access to the mechanism, the experiments were carried out as shown in Scheme 3. When the



b: R = H; **3b** (50%), **2b** (35%)
j: R = Me; **3j** (58%), **2j** (33%)
i: R = Ph; **3i** (0%), **2i** (89%)

Scheme 2

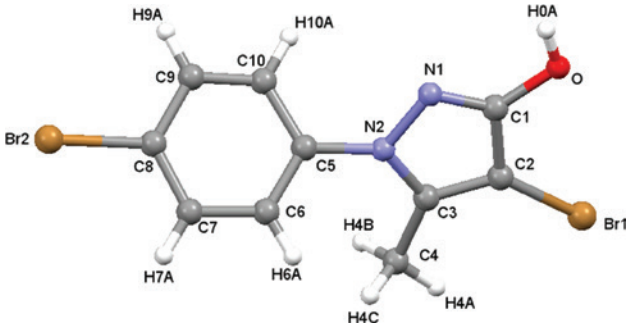
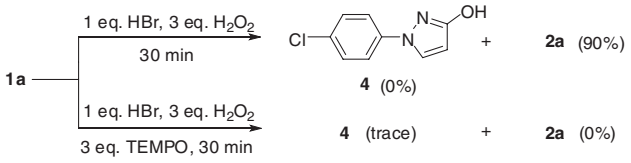
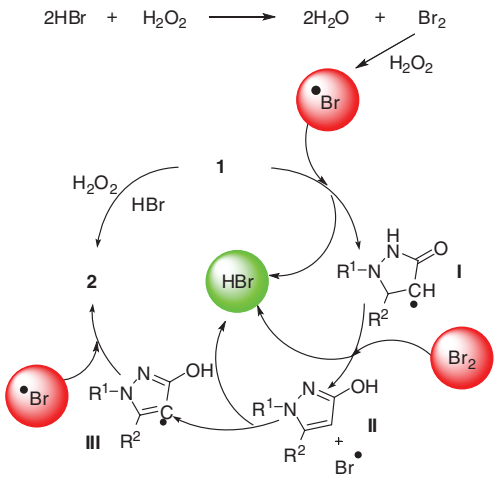


Figure 1 Molecular structure of **3j** with atom labeling.



Scheme 3



Scheme 4

reaction under optimized conditions was performed in the presence of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) as a radical scavenger, only a trace amount of 1-(4-chlorophenyl)-1*H*-pyrazol-3-ol (**4**) was detected, suggesting a radical pathway. This finding and previous reports [25–27], are consistent with the mechanism suggested in Scheme 4. First, compound **1** undergoes a reaction with a bromine radical to generate the corresponding radical intermediate **I**, which is subsequently converted to the substituted pyrazol-3-ol **II** by oxidation with molecular bromine. Then, in the presence of the bromine radical, the corresponding radical species **III** is generated from the intermediate compound **II**. Finally, the reaction of the intermediate product **III** with the bromide radical furnishes the observed 4-bromopyrazol-3-ol **2**.

Conclusions

A green and efficient protocol to prepare substituted 4-bromo-pyrazol-3-ols **2** from pyrazolidin-3-ones **1** under mild conditions in excellent yields was described. The corresponding dibromination products **3b,j** were also obtained in moderate yields under harsh conditions.

Experimental

Proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained on a Bruker spectrometer operating at 600 MHz with dimethyl sulfoxide-d_6 as solvent and tetramethylsilane as internal standard. Infrared (IR) spectra were obtained using KBr disks on a Bomem Michelson Series Fourier-transform infrared spectrometer. The mass spectrometry (MS) data were recorded with an Agilent 7890A-5975C instrument. Melting points were obtained on an X-4 microscope electrothermal apparatus (Taike, China) and are uncorrected. Elemental analyses were carried out on a Vario EL III analyzer. Spectral data for compounds **2b**, **3b** and **4** are virtually identical with the reported values [9, 20, 28].

Synthesis of 4-bromopyrazol-3-ones 2a–l

A mixture of **1a–l** (0.01 mol) in $CHCl_3$ (10 mL) and 40% hydrobromic acid (40%, 0.01 mol) was stirred at 60°C and treated dropwise for 10 min with an aqueous solution of H_2O_2 (30%, 0.03 mol), and stirring was continued for an additional 20 min. The resultant precipitate of **2a–l** was filtered off and crystallized from ethanol. The filtrate was concentrated and the residue was subjected to silica gel chromatography eluting with ethyl acetate/petroleum ether (10:1) to give an additional amount of **2a–l**.

4-Bromo-1-(4-chlorophenyl)-1*H*-pyrazole-3-ol (2a) White solid; mp 192–194°C; yield 90%; ^{1}H NMR: δ 11.13 (s, 1H, OH), 8.58 (s, 1H, CH), 7.71 (d, J = 9 Hz, 2H, Ar), 7.51 (d, J = 9 Hz, 2H, Ar); IR: 3440, 2971, 1617, 1563, 1494, 1392, 1306, 1105 cm^{-1}; MS: m/z 274.3 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_9H_6BrClN_2O$: C, 39.52; H, 2.21; N, 10.24. Found: C, 39.81; H, 2.03; N, 10.02.

4-Bromo-1-phenyl-1*H*-pyrazole-3-ol (2b) Yellow solid; mp 188–190°C; yield 91%; ^{1}H NMR: δ 11.02 (s, 1H, OH), 8.54 (s, 1H, CH), 7.69 (d, J = 8 Hz, 2H, Ar), 7.45 (t, J = 8 Hz, 2H, Ar), 7.23 (t, J = 8 Hz, 1H, Ar); IR: 3449, 2927, 1620, 1550, 1493, 1309, 1102 cm^{-1}; MS: m/z 240.1 [(M + 1)$^+$, 100%].

4-Bromo-1-(4-fluorophenyl)-1*H*-pyrazole-3-ol (2c) White solid; mp 219–221°C; yield 89%; ^{1}H NMR: δ 11.01 (s, 1H, OH), 8.51 (s, 1H, CH), 7.70 (m, 2H, Ar), 7.30 (t, J = 9 Hz, 2H, Ar); IR: 3451, 2971, 1622, 1568, 1519, 1404, 1311, 1240, 1087 cm^{-1}; MS: m/z 258.1 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_9H_6BrFN_2O$: C, 42.05; H, 2.35; N, 10.90. Found: C, 42.22; H, 2.21; N, 10.68.

4-Bromo-1-(4-methylphenyl)-1*H*-pyrazole-3-ol (2d) Yellow solid; mp 183–185°C; yield 92%; ^{1}H NMR: δ 10.93 (s, 1H, OH), 8.47 (s, 1H, CH), 7.56 (d, J = 8 Hz, 2H, Ar), 7.24 (d, J = 8 Hz, 2H, Ar), 2.31 (s, 3H, CH_3); IR: 3454, 2964, 1625, 1548, 1381, 1327, 1082 cm^{-1}; MS: m/z 254.2 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_{10}H_9BrN_2O$: C, 47.46; H, 3.58; N, 11.07. Found: C, 47.31; H, 3.73; N, 10.88.

4-Bromo-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-3-ol (2e) Yellow solid; mp 233–235°C; yield 91%; ^{1}H NMR: δ 11.48 (s, 1H, OH), 8.49 (s, 1H, CH), 7.98 (d, J = 8 Hz, 1H, Ar), 7.60 (d, J = 8 Hz, 1H, Ar), 7.37 (d, J = 8 Hz, 1H, Ar); IR: 3451, 2965, 1626, 1582, 1444, 1389, 1305, 1261, 1068 cm^{-1}; MS: m/z 273.1 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_8H_5BrClN_3O$: C, 35.00; H, 1.84; N, 15.31. Found: C, 34.83; H, 2.02; N, 15.50.

4-Bromo-5-methyl-1-(4-chlorophenyl)-1*H*-pyrazol-3-ol (2f) Yellow solid; mp 221–223°C; yield 92%; ^{1}H NMR: δ 10.80 (s, 1H, OH), 7.55 (m, 2H, Ar), 7.51 (m, 2H, Ar), 2.28 (s, 3H, CH_3); IR: 3455, 2978, 1617, 1545, 1510, 1393, 1102 cm^{-1}; MS: m/z 288.2 [(M + 1)$^+$, 81%]. Anal. Calcd for $C_{10}H_8BrClN_2O$: C, 41.77; H, 2.80; N, 9.74. Found: C, 41.61; H, 2.93; N, 9.89.

4-Bromo-5-phenyl-1-(4-chlorophenyl)-1*H*-pyrazol-3-ol (2g) White solid; mp 253–255°C; yield 94%; ^{1}H NMR: δ 11.07 (s, 1H, OH), 7.43 (m, 3H, Ar), 7.39 (d, J = 9 Hz, 2H, Ar), 7.30 (m, 2H, Ar), 7.21 (d, J = 9 Hz, 2H, Ar); IR: 3462, 2973, 1552, 1496, 1331, 1075 cm^{-1}; MS: m/z 350.3 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_{15}H_{10}BrClN_2O$: C, 51.53; H, 2.88; N, 8.01. Found: C, 51.34; H, 3.06; N, 8.22.

4-Bromo-5-methoxy-1-(4-chlorophenyl)-1*H*-pyrazol-3-ol (2h) Yellow solid; mp 228–230°C; yield 95%; ^{1}H NMR: δ 11.37 (s, 1H, OH), 7.65 (m, 2H, Ar), 7.38 (m, 2H, Ar), 3.74 (s, 3H, OCH_3); IR: 3452, 2961, 1632, 1560, 1503, 1402, 1314, 1207, 1054 cm^{-1}; MS: m/z 300.4 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_{10}H_8BrClN_2O_2$: C, 39.57; H, 2.66; N, 9.23. Found: C, 39.48; H, 2.79; N, 9.38.

4-Bromo-1,5-diphenyl-1*H*-pyrazol-3-ol (2i) Yellow solid; mp 242–244°C; yield 93%; ^{1}H NMR: δ 10.98 (s, 1H, OH), 7.41 (m, 3H, Ar), 7.29 (m, 5H, Ar), 7.14 (d, J = 8 Hz, 2H, Ar); IR: 3453, 2965, 1624, 1541, 1444, 1335, 1252, 1085 cm^{-1}; MS: m/z 314.1 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_{15}H_{11}BrN_2O$: C, 57.16; H, 3.52; N, 8.89. Found: C, 57.37; H, 3.38; N, 8.71.

4-Bromo-5-methyl-1-phenyl-1*H*-pyrazol-3-ol (2j) White solid; mp 218–220°C; yield 91%; ^{1}H NMR: δ 10.71 (s, 1H, OH), 7.49 (m, 4H, Ar), 7.36 (t, J = 7 Hz, 1H, Ar), 2.27 (s, 3H, CH_3); IR: 3450, 2969, 1623, 1549, 1496, 1409, 1328, 1270, 1103 cm^{-1}; MS: m/z 254.1 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_{10}H_9BrN_2O$: C, 47.46; H, 3.58; N, 11.07. Found: C, 47.63; H, 3.81; N, 10.86.

4-Bromo-5-methyl-1-(4-methylphenyl)-1*H*-pyrazol-3-ol (2k) White solid; mp 232–234°C; yield 92%; ^{1}H NMR: δ 10.64 (s, 1H, OH), 7.35–7.28 (m, 4H, Ar), 2.35 (s, 3H, CH_3), 2.24 (s, 3H, CH_3); IR: 3452, 2974, 1627, 1553, 1515, 1406, 1323, 1257, 1103 cm^{-1}; MS: m/z 266.1 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_{11}H_{11}BrN_2O$: C, 49.46; H, 4.15; N, 10.49. Found: C, 49.63; H, 4.36; N, 10.06.

4-Bromo-5-methyl-1*H*-pyrazol-3-ol (2l) White solid; mp 192–194°C; yield 85%; ^{1}H NMR: δ 2.09 (s, 3H, CH); IR: 2060–3270, 1587, 1253, 1172, 1053 cm^{-1}; MS: m/z 176.9659 [(M + 1)$^+$, 100%). Anal. Calcd for $C_4H_5BrN_2O$: C, 27.14; H, 2.85; N, 15.83. Found: C, 27.26; H, 2.96; N, 15.66.

Synthesis of 4-bromo-1-(4-bromophenyl)pyrazol-3-ones 3b,j

A mixture of **1b,j** (0.01 mol), CCl_4 (10 mL) and hydrobromic acid (40%, 0.05 mol) was stirred, heated under reflux and treated dropwise with an aqueous solution of H_2O_2 (30%, 0.08 mol) for 3 h. After concentration under reduced pressure, the residue was chromatographed on silica gel eluting with ethyl acetate/petroleum ether (10:1) to give **3b,j**.

4-Bromo-1-(4-bromophenyl)-1*H*-pyrazole-3-ol (3b) Yellow solid; mp 199–201°C; yield 50%; ^{1}H NMR: δ 11.17 (s, 1H, OH), 8.62 (s, 1H, CH), 7.69 (m, 4H, Ar); IR: 3458, 2962, 1624, 1556, 1494, 1390, 1302, 1209, 1048 cm^{-1}; MS: m/z 318.9 [(M + 1)$^+$, 100%].

4-Bromo-5-methyl-1-(4-bromophenyl)-1*H*-pyrazol-3-ol (3j) White solid; mp 243–245°C; yield 58%; ^{1}H NMR: δ 10.82 (s, 1H, OH), 7.68 (d, *J* = 9 Hz, 2H, Ar), 7.45 (d, *J* = 9 Hz, 2H, Ar), 2.28 (s, 3H, CH_3); IR: 3446, 2971, 1628, 1547, 1510, 1395, 1322, 1261, 1108 cm^{-1}; MS: *m/z* 330.3 [(M + 1)$^+$, 100%]. Anal. Calcd for $C_{10}H_8Br_2N_2O$: C, 36.18; H, 2.43; N, 8.44. Found: C, 36.33; H, 2.61; N, 8.28.

1-(4-Chlorophenyl)-1*H*-pyrazol-3-ol (4) White solid; mp 189–191°C; ^{1}H NMR: δ 10.32 (s, 1H, OH), 8.24 (d, *J* = 3 Hz, 1H, CH), 7.70 (d, *J* = 9 Hz, 2H, Ar), 7.48 (d, *J* = 9 Hz, 2H, Ar), 5.84 (d, *J* = 3 Hz, 1H, CH); IR: 3438, 2976, 1630, 1545, 1489, 1382, 1245, 1057, 945, 757 cm^{-1}; MS: *m/z* 195.7 [(M + 1)$^+$, 100%].

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References

[1] Rapposelli, S.; Lapucci, A.; Minutolo, F.; Orlandini, E.; Ortore, G.; Pinza, M.; Balsamo, A. Synthesis and COX-2 inhibitory properties of *N*-phenyl and *N*-benzyl-substituted amides of 2-(4-methylsulfonylphenyl)cyclopent-1-ene-1-carboxylic acid and of their pyrazole, thiophene and isoxazole analogs. *Farmaco* **2004**, *59*, 25–31.

[2] Cottineau, B.; Toto, P.; Marot, C.; Pipaud, A.; Chenault, J. Synthesis and hypoglycemic evaluation of substituted pyrazole-4-carboxylic acids. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 2105–2108.

[3] Al-Omran, F.; El-Khair, A. A. Synthesis of polyfunctionally substituted heteroaromatic compounds via benzotriazolyl chalcones with antimicrobial and antifungal activities. *J. Heterocycl. Chem.* **2004**, *41*, 327–333.

[4] Sechi, M.; Sannia, L.; Carta, F.; Palomba, M.; Dallocchio, R.; Dessì, A.; Derudas, M.; Zawahir, Z.; Neamati, N. Design of novel bioisosteres of β-diketo acid inhibitors of HIV-1 integrase. *Antiviral Chem. Chemother.* **2005**, *16*, 41–61.

[5] Morita, H.; Harada, K.; Okamoto, Y.; Takagi, K. Ring transformation of 3-halo-4-methoxycoumarins into pyrazoles with hydrazines. *J. Heterocycl. Chem.* **1999**, *36*, 767–770.

[6] Li, Y.; Liu, Y. Y.; Chen, N. Q.; Lü, K. Z.; Xiong, X. H.; Li, J. One-pot regioselective synthesis of novel oximino ester-containing 1-aryl-4-chloro-3-oxypyrazoles as potential fungicides. *Helv. Chim. Acta* **2014**, *97*, 1269–1282.

[7] Arbačiauskienė, E.; Vilkauskaitė, G.; Eller, G. A.; Holzer, W.; Šačkus, A. Pd-catalyzed cross-coupling reactions of halogenated 1-phenylpyrazol-3-ols and related triflates. *Tetrahedron* **2009**, *65*, 7817–7824.

[8] Arbačiauskienė, E.; Martynaitis, V.; Krikštolaitytė, S.; Holzer, W.; Šačkus, A. Synthesis of 3-substituted 1-phenyl-1*H*-pyrazole-4-carbaldehydes and the corresponding ethanones by Pd-catalysed cross-coupling reactions. *Arkivoc* **2011**, *11*, 1–21.

[9] Nedzelskytė, E.; Martynaitis, V.; Šačkus, A.; Eller, G. A.; Holzer, W. Synthesis of mono-and dibromo-derivatives of 1-phenylpyrazol-3-ol. *Molbank* **2007**, *3*, M551.

[10] Jørgensen, L.; Nielsen, B.; Pickering, D. S.; Kristensen, A. S.; Frydenvang, K.; Madsen, U.; Clausen, R. P. Analogues of 3-hydroxyisoxazole-containing glutamate receptor ligands based on the 3-hydroxypyrazole-moiety: design, synthesis and pharmacological characterization. *Neurochem. Res.* **2014**, *39*, 1895–1905.

[11] Arbačiauskienė, E.; Kazlauskas, K.; Miasojedovas, A.; Juršėnas, S.; Jankauskas, V.; Holzer, W.; Getautis, V.; Šačkus, A. Multifunctional polyconjugated molecules with carbazolyl and pyrazolyl moieties for optoelectronic applications. *Synth. Met.* **2010**, *160*, 490–498.

[12] Arbačiauskienė, E.; Kazlauskas, K.; Miasojedovas, A.; Juršėnas, S.; Jankauskas, V.; Holzer, W.; Getautis, V.; Šačkus, A. Pyrazolyl-substituted polyconjugated molecules for optoelectronic applications. *Dyes Pigments* **2010**, *85*, 79–85.

[13] Chande, M. S.; Bhandari, J. D.; Joshi, V. R. Investigation on the reaction of 4-anilino-5-mercapto-s-triazoles with pyrazolines and barbituric Acids. *Indian J. Chem. B* **1993**, *32B*, 1218–1228.

[14] El-Saraf, G. A.; El-Sayed, A. M.; El-Saghier, A. M. One-pot PTC synthesis of polyfused pyrazoles. *Heteroat. Chem.* **2003**, *14*, 211–217.

[15] Vogel, A. Vogel's Practical Organic Chemistry; Longman: London, 1978.

[16] Ahmed, S. A.; Awad, I. M.; Abdel-Wahab, A. M. A. A highly efficient photochemical bromination as a new method for preparation of mono, bis and fused pyrazole derivatives. *Photochem. Photobiol. Sci.* **2002**, *1*, 84–86.

[17] Huang, Y. Y.; Lin, H. C.; Cheng, K. M.; Su, W. N.; Sung, K. C.; Lin, T. P.; Huang, J. J.; Lin, S. K.; Wong, F. F. Efficient di-bromination of 5-pyrazolones and 5-hydroxypyrazoles by *N*-bromobenzamide. *Tetrahedron* **2009**, *65*, 9592–9597.

[18] Cheng, K. M.; Wu, J. B.; Lin, H. C.; Huang, J. J.; Huang, Y. Y.; Lin, S. K.; Lin, T. P.; Wong, F. F. Dibromination of 5-pyrazolones and 5-hydroxypyrazoles via dibromoisocyanuric acid. *J. Heterocycl. Chem.* **2010**, *47*, 1153–1156.

[19] Frigola, J.; Colombo, A.; Pares, J.; Martinez, L.; Sagarra, R.; Roser, R. Synthesis, structure and inhibitory effects on cyclooxygenase, lipoxygenase, thromboxane synthetase and platelet aggregation of 3-amino-4, 5-dihydro-1H-pyrazole derivatives. *Eur. J. Med. Chem.* **1989**, *24*, 435–445.

[20] Li, Y.; Liu, R.; Yan, Z.; Zhang, X.; Zhu, H. Synthesis, crystal structure and fungicidal activities of new type oxazolidinone-based strobilurin analogues. *Bull. Korean Chem. Soc.* **2010**, *31*, 3341–3347.

[21] Liu, Y.; Li, Y.; Chen, N.; Xiong, X.; Yu, L.; Jing, C.; Zheng, Q.; Du, K.; Jiang, H. Synthesis, crystal structure, and fungicidal activity of novel 1-aryl-3-oxypyrazoles containing a Z-configuration methyl 2-(methoxyimino) acetate moiety. *J. Chem. Res.* **2014**, *38*, 520–523.

[22] Liu, Y.; Shi, H.; Li, Y.; Zhu, H. Synthesis, crystal structure, and fungicidal activity of novel 1, 5-diaryl-1*H*-pyrazol-3-oxyacetate derivatives. *J. Heterocycl. Chem.* **2010**, *47*, 897–902.

[23] Mercader, J. V.; Agulló, C.; Abad-Somovilla, A.; Abad-Fuentes, A. Synthesis of site-heterologous haptens for high-affinity anti-pyraclostrobin antibody generation. *Org. Biomol. Chem.* **2011**, *9*, 1443–1453.

[24] Saikia, I.; Borah, A. J.; Phukan, P. Use of bromine and bromo-organic compounds in organic synthesis. *Chem. Rev.* **2016**, *116*, 6837–7042.

[25] Samanta, S.; Pappula, V.; Dinda, M.; Adimurthy, S. Transition metal-free oxidative esterification of benzylic alcohols in aqueous medium. *Org. Biomol. Chem.* **2014**, *12*, 9453–9456.
[26] Ghaffarzadeh, M.; Bolourtchian, M.; Tabar-Heydar, K.; Daryaei, I.; Mohsenzadeh, F. H_2O_2-HBr: a metal-free and organic solvent-free reagent system for the synthesis of arylaldehydes from methylarenes. *J. Chem. Sci.* **2009**, *121*, 177–182.
[27] Khan, A. T.; Parvin, T.; Choudhury, L. H.; Ghosh, S. A simple synthetic protocol for oxidation of alkyl-arenes into ketones using a combination of HBr–H_2O_2. *Tetrahedron Lett.* **2007**, *48*, 2271–2274.
[28] O'Brien, D.; Gates Jr, J. Some reactions of 3-hydroxy-1-phenylpyrazole. *J. Org. Chem.* **1966**, *31*, 1538–1542.

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