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PAPER

Atmospheric CO_2 Promoted Synthesis of N-Containing Heterocycles over $B(C_6F_5)_3$ Catalyst

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$B(C_6F_5)_3$ combined with atmospheric CO_2 was found to be highly effective for the cyclization of ortho-substituted aniline derivatives with N,N-dimethylformamide (DMF), and a series of N-containing heterocycles including benzothiazoles, benzomidazoles, quinazolinone and benzoxazole were obtained in good to excellent yields.

1. Introduction

Since CO_2 emission has caused serious environmental problems, the capture and utilization of CO_2 have drawn much attention in recent years.[1] As an abundant, nontoxic, easily available, and renewable carbon source, CO_2 can be widely applied in many areas such as food, separation, chemical reaction, material processing and fabrication, and so on. Recently, the CO_2-promoted reactions have been reported, showing promising potentials for applications of CO_2.[2] For example, Kleij et al. reported a CO_2-based method for efficient and highly selective formation of cyclic cis-diol scaffolds.[3] Jiang's group found that the side reaction in the oxidative cross-coupling of sulfides could be suppressed efficiently in the presence of CO_2.[4] Wang et al. reported a CO_2-mediated metathesis reaction of amines with N,N-dimethylformamide to various formamides.[5] Our group applied CO_2 as a cocatalyst combined with a task-specific ionic liquid to realize the efficient hydration of propargylic alcohols to α-hydroxy ketones.[6] As a promotor or cocatalyst, CO_2 could be easily separated from the reaction solution, thus showing promising applications.

N-containing heterocyclic compounds are generally biocompatible, which could be widely used as pharmaceutical and agrochemical agents.[7] The scaffolds of benzazoles, such as benzothiazoles, benzimidazoles, quinazolinones and benzoxazoles, are typical N-containing heterocycles that are extensively used as antiviral, antibacterial, anticancer, antihistaminic, antitubercular, antihypertensive, anti-inflammatory agents and plant growth regulators.[8] The general protocols for the synthesis of these N-containing heterocycles are based on the condensation reaction of ortho-substituted aniline derivatives with carboxylic acids,[9] nitriles[10] and esters,[11] or the oxidative cyclization of the substrates with aldehydes[12] and alcohols[13] in the presence of oxidants. Recently, the synthesis of benzimidazoles via the reaction of 1,2-arylenediamines with N,N-dimethylformamide (DMF) was reported, however, highly acidic reaction medium was required.[14] The synthesis of N-containing heterocyclic compounds from *o*-phenylenediamines and N-substituted formamide was also reported using zinc catalyst in the presence of poly(methylhydrosiloxane).[15] Most of the reported protocols suffered from one or more drawbacks such as metal-based or toxic catalyst systems, strong oxidising or caustic reagents, hazardous solvents, poor yield and low selectivity. Therefore, exploring simple, green, efficient catalytic systems is still highly desirable.

Herein, we present an efficient protocol for the synthesis of N-containing heterocycles, which was realized by CO_2-promoted cyclization of ortho-substituted aniline derivatives (including 2-aminothiophenols, *o*-phenylenediamines, anthranilamide and 2-aminophenol) with N,N-dimethylformamide (DMF) over $B(C_6F_5)_3$ catalyst under mild conditions. A series of N-containing heterocycles including benzothiazoles, benzomidazoles, quinazolinone and benzoxazole were obtained in good to excellent yields. The reaction mechanism was explored in details.

2. Experimental section

2.1 Materials

CO_2 (99.99%) was provided by Beijing Analytical Instrument Company. 2-Aminothiophenol (98%) and 2-amino-4-chlorothiophenol (97%) were purchased from J&K Scientific Ltd. 2-Amino-4-methoxybenzenethiol (98%), 2-amino-5-nitrobenzenethiol (98%) were purchased from Beijing Kaida Technology Development Co., Ltd. 2-Amino-5-methylbenzenethiol, 2-amino-5-methoxybenzenethiol, 2-amino-5-ethoxybenzenethiol, 2-amino-5-fluorobenzenethiol, 2-amino-5-chlorobenzenethiol and 2-amino-5-

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bromobenzenethiol were synthesized according to the reported procedures.[S1-6] Different kinds of o-phenylenediamines and hydrosilanes were purchased from J&K Scientific Ltd and Alfa Aesar. The deuterated solvents (DMSO-d_6, C_6D_6, $CDCl_3$, DMF-d_7) were obtained from Cambridge Isotope Laboratories, Inc. All chemicals were of analytical grade and used as received.

2.2 Typical procedure for the cyclization of ortho-substituted aniline derivatives with CO_2

In a typical experiment, 2-aminothiophenol (0.5 mmol, 0.0626 g), $B(C_6F_5)_3$ (5 mol%, 0.0128 g), Et_2SiH_2 (2 mmol, 0.1764 g), DMF (1 mL) were loaded in a 10 mL flask equipped with a magnetic stirrer. The air in the reactor was replaced by CO_2. The CO_2 pressure was kept at 0.1 MPa using a balloon. The reaction mixture was stirred at 120 °C for 24 h. Finally, the reaction mixture was cooled down in ice-water, and the product yields were determined by ^{1}H NMR using pyrazine as the internal standard of the crude mixture. The pure products were obtained via column chromatography separation and characterized by NMR. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) analysis was carried out on a Bruker Avance Ⅲ 400 HD spectrometer with DMSO-d_6 as the solvent at ambient temperature. The NMR spectra of the products were given in Supporting Information (Figure S3-S33).

2.3 NMR spectral data of the products

1a: benzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 9.41 (s, 1H), 8.12 (dd, *J* = 8.1, 2.8 Hz, 2H), 7.48 (m, 2H); ^{13}C NMR (100 MHz, DMSO) δ 156.26, 153.50, 134.03, 126.50, 125.80, 123.48, 122.79.

1b: 5-methylbenzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 9.29 (s, 1H), 8.04-7.84 (m, 2H), 7.33 (d, *J* = 7.8 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 155.24, 151.71, 135.62, 134.19, 128.13, 123.00, 122.35, 21.44.

1c: 5-methoxybenzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 9.18 (s, 1H), 7.96 (d, *J* = 8.9 Hz, 1H), 7.72 (d, *J* = 2.5 Hz, 1H), 7.13 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 157.97, 153.78, 148.01, 135.53, 123.89, 116.15, 105.20, 56.17.

1d: 6-methoxybenzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 8.34 (s, 1H), 7.87 (s, 1H), 7.04 (d, J = 8.6 Hz, 1H), 6.62 (d, J = 8.4 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 162.07, 161.37, 140.89, 137.85, 115.79, 110.49, 108.09, 56.07.

1e: 5-ethoxybenzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 9.18 (s, 1H), 7.95 (d, *J* = 8.9 Hz, 1H), 7.69 (d, *J* = 2.4 Hz, 1H), 7.11 (dd, *J* = 8.9, 2.5 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 1.36 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 157.19, 153.69, 147.92, 135.51, 123.88, 116.43, 105.77, 64.15, 15.08.

1f: 5-fluorobenzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 9.37 (s, 1H), 8.26 – 8.01 (m, 2H), 7.42 (td, *J* = 9.0, 2.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 161.59, 159.17, 156.87, 156.84, 150.40, 135.46, 135.35, 124.77, 124.67, 115.38, 115.13, 109.30, 109.03.

1g: 5-chlorobenzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 9.42 (s, 1H), 8.34 (d, *J* = 2.0 Hz, 1H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.58 (dd, *J* = 8.7, 2.1 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 157.81, 152.31, 135.74, 130.57, 127.16, 124.67, 122.66.

1h: 6-chlorobenzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 9.47 (s, 1H), 8.19 (dd, *J* = 16.2, 5.2 Hz, 2H), 7.54 (dd, *J* = 8.6, 1.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 159.10, 154.47, 132.93, 131.49, 126.11, 124.48, 122.96.

1i: 5-bromobenzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 9.40 (s, 1H), 8.47 (d, *J* = 1.8 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 1H), 7.69 (dd, *J* = 8.7, 1.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 157.79, 152.57, 136.22, 129.83, 125.55, 125.03, 118.73.

1j: 5-nitrobenzothiazole: ^{1}H NMR (400 MHz, DMSO) δ 9.72 (s, 1H), 9.24 (d, *J* = 1.9 Hz, 1H), 8.38 – 8.32 (m, 1H), 8.27 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 163.59, 157.13, 145.18, 134.99, 124.02, 121.82, 120.20.

2a: benzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.47 (s, 1H), 8.22 (s, 1H), 7.59 (s, 2H), 7.19 (dd, *J* = 5.9, 3.1 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ 142.37, 122.15.

2b: 6-methylbenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.30 (s, 1H), 8.12 (s, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.36 (s, 1H), 7.00 (d, *J* = 8.2 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 139.44, 136.43, 135.37, 131.80, 123.43, 114.54, 113.84, 20.68.

2c: 7-methylbenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.41 (s, 1H), 8.15 (s, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H); ^{13}C NMR (101 MHz, DMSO) δ 141.72, 137.96, 132.02, 129.16, 122.41, 122.14, 113.11, 17.21.

2d: 5, 6-dimethylbenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.23 (s, 1H), 8.07 (s, 1H), 7.36 (s, 2H), 2.30 (s, 6H); ^{13}C NMR (100 MHz, DMSO) δ 140.51, 136.20, 129.61, 114.81, 19.44.

2e: 6-methoxybenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.28 (s, 1H), 8.10 (s, 1H), 7.46 (s, 1H), 7.08 (d, *J* = 2.0 Hz, 1H), 6.81 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 156.05, 141.92, 138.41, 133.94, 116.77, 111.82, 97.91, 55.87.

2f: 5-fluorobenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.81 (s, 1H), 8.38 (s, 1H), 7.63 (dd, *J* = 8.5, 4.9 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.04 (td, *J* = 9.7, 1.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 159.46, 157.12, 143.01, 115.70, 109.74, 109.49, 100.93 (CH).

2g: 5-chlorobenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.61 (s, 1H), 8.27 (s, 1H), 7.65 (s, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.21 (dd, *J* = 8.5, J = 1.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 143.46, 139.29, 136.62, 126.19, 122.04, 116.39, 115.22.

2h: 5, 6-dichlorobenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.72 (s, 1H), 8.34 (s, 1H), 7.86 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 145.2, 138.2, 124.8, 117.2.

2i: 5-bromobenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.70 (s, 1H), 8.31 (s, 1H), 7.83 (s, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 1H);^{13}C NMR (100 MHz, DMSO) δ 143.69, 125.05, 114.50.

2j: 5-nitrobenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 8.55 (s, 1H), 8.51 (d, *J* = 2.1 Hz, 1H), 8.11 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.76 (d, *J* = 8.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 146.26, 142.15, 117.10.

2k: 5-trifluoromethylbenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.89 (s, 1H), 8.45 (s, 1H), 7.97 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 8.5, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 144.27, 128.67, 125.97, 123.27, 122.27, 121.95, 120.57, 118.03.

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2l: methyl benzimidazole-5-carboxylate: ^{1}H NMR (400 MHz, DMSO) δ 12.77 (s, 1H), 8.40 (s, 1H), 8.23 (s, 1H), 7.84 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 167.28, 145.07, 123.72, 123.39, 52.39.

2m: etheyl benzimidazole-5-carboxylate: ^{1}H NMR (400 MHz, DMSO) δ 11.73 (s, 1H), 8.43 (s, 1H), 8.24 (s, 1H), 7.84 (dd, *J* = 8.5, *J* = 1.3 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 166.51, 144.82, 141.22, 138.44, 123.80, 123.18, 117.77, 115.12, 60.69, 14.45.

2n: 5-benzoylbenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.91 (s, 1H), 8.49 (s, 1H), 8.04 (s, 1H), 7.83 – 7.65 (m, 4H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ 195.34, 155.18, 144.37, 137.73, 133.67, 131.51, 130.49, 129.02, 127.88, 123.41, 109.43, 107.55.

2o: N-methylbenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 8.19 (s, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.24 (dd, *J* = 14.3, 7.7 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 143.95, 142.74, 134.03, 121.68, 120.88, 118.71, 109.57, 30.06

2p: N-phenylbenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 8.08 (s, 1H), 7.89 – 7.87 (m, 1H), 7.53 – 7.41 (m, 6H), 7.30 (dd, *J* = 9.1, *J* =5.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ 142.73, 135.25, 132.70, 129.06, 127.12, 123.08, 122.81, 121.92, 119.47, 109.54.

2q: 4-azabenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.78 (s, 1H), 8.45 (s, 1H), 8.35 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.02 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.23 (dd, *J* = 8.0, 4.7 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 151.50, 144.37, 144.17, 131.09, 124.41, 118.19.

2r: 5-azabenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.86 (s, 1H), 8.95 (s, 1H), 8.40 (s, 1H), 8.30 (d, *J* = 5.5 Hz, 1H), 7.59 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 144.63, 141.61, 141.32, 140.12, 138.06, 109.80.

2s: 5-azabenzimidazole: ^{1}H NMR (400 MHz, DMSO) δ 12.51 (s, 1H), 8.47 (s, 1H), 8.11 (s, 2H), 8.00 (dd, *J* = 6.3, 3.3 Hz, 2H), 7.37 (dd, *J* = 6.4, 3.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ146.95, 132.01, 130.18, 129.16, 128.25, 123.79.

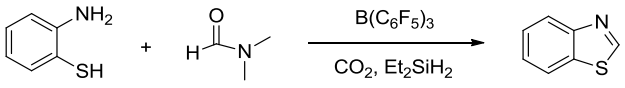
3a: quinazolinone benzoxazole: ^{1}H NMR (400 MHz, DMSO) δ 12.24 (s, 1H), 8.25 – 7.98 (m, 2H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 161.19, 149.24, 145.84, 134.77, 127.69, 127.20, 126.30, 123.11.

4a: benzoxazole: ^{1}H NMR (400 MHz, DMSO) δ 8.71 (s, 1H), 7.86 – 7.71 (m, 1H), 7.71 – 7.56 (m, 1H), 7.33 (td, *J* = 7.0, 1.4 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 153.75, 149.26, 139.60, 125.21, 124.22, 119.88, 110.72.

3. Results and discussion

In our initial experiments, the cyclization of 2-aminothiophenol catalysed by $B(C_6F_5)_3$ as a model reaction was carried out, and the results are listed in Table 1. The cyclization reaction did not occur in the presence of atmospheric CO_2 without DMF, while it could proceed in the presence of DMF without CO_2, producing benzothiazole in a yield of 23% (Table 1, entries 1-2). Excitingly, the coexistence of atmospheric CO_2 and DMF significantly improved the reaction activity, affording benzothiazole in an excellent yield of 99% under the similar conditions (Table 1, entry 3). The above results indicated that DMF involved the synthesis of the product, and CO_2 greatly promoted the reaction (Table 1, entries 2 vs. 3). Then the influence of the catalyst amount was tested, and benzothiazole could be obtained in good yields even with 1 mol% $B(C_6F_5)_3$ (Table 1, entry 5), demonstrating that $B(C_6F_5)_3$ combined with atmospheric CO_2 was highly efficient for this reaction. The influences of reaction temperature and time were also investigated. It was indicated that the yields of benzothiazole decreased obviously as decreasing the temperature (Table 1, entries 3 vs. 6, 7) or shortening the time (Table 1, entries 3 vs. 8-10), and the optimal conditions were 120 °C and 24 h.

Table 1. The cyclization of 2-aminothiophenol with DMF under different conditions[a]

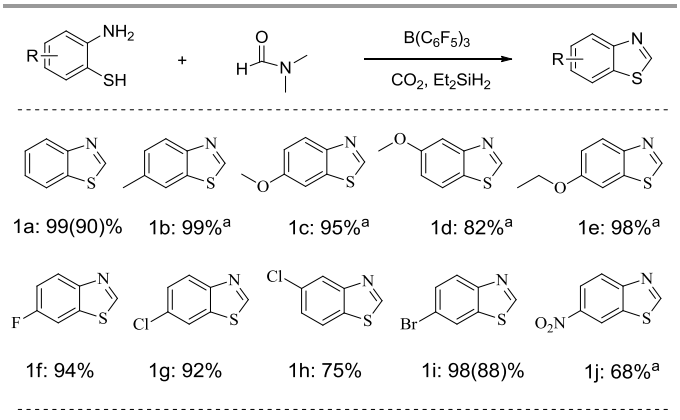


Entry	Cats/mol%	T/°C	t/h	Conv. [%][b]	Yield [%][b]
1[c]	5	120	24	0	0
2[d]	5	120	24	26	23
3	5	120	24	>99	99
4	3	120	24	99	92
5	1	120	24	76	73
6	5	100	24	51	50
7	5	80	24	30	26
8	5	120	18	98	90
9	5	120	12	69	66
10	5	120	6	15	10

[a]Reaction conditions: 2-aminothiophenol (0.5 mmol), $B(C_6F_5)_3$ (5 mol%), Et_2SiH_2 (2 mmol), DMF (1 mL), CO_2 (0.1 MPa), 120 °C, 24 h; [b]determined by ^{1}H NMR (DMSO-d_6, 400 MHz) using pyrazine as an internal standard; [c]only CO_2 (0.1 MPa), without DMF; [d]only DMF (1 mL), without CO_2.

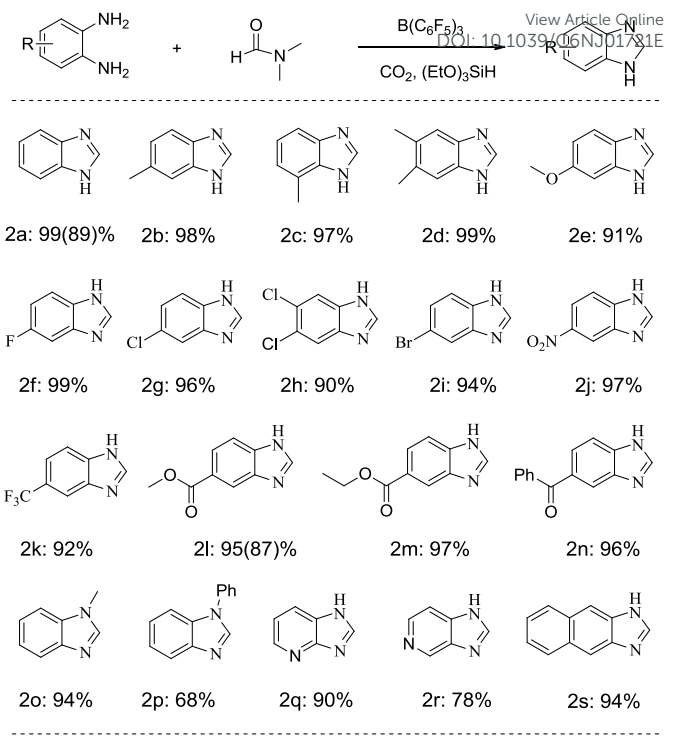
Based on the above results, the substituted 2-aminothiophenols with electron donating and electron withdrawing groups were tested to react with DMF in the presence of atmospheric CO_2 and Et_2SiH_2 over $B(C_6F_5)_3$ catalyst. As shown in Scheme 1, all the substituted substrates could be converted to corresponding benzothiazoles, and excellent product yields were gained in most cases. Though the reactivities of the substrates with electron donating groups were lower than those with electron withdrawing groups, high product yields could be obtained as reaction time prolonged to 40 h (Scheme 1, 1b-e). The derivatives with electron withdrawing groups including -F, -Cl and -Br displayed relatively high reactivities, and corresponding products were achieved in high yields (Scheme 1, 1f-i). Even for the substrate with strong electron withdrawing -NO_2 group, corresponding product, 5-nitrobenzothiazole, was obtained in a yield of 68% within 40 h (Scheme 1, 1j). In addition, 4-substituent 2-aminothiophenols were also tolerated in this reaction, though

less reactive than 5-substituent substrates, probably due to electronic and steric effects (Scheme 1, 1d, 1h vs. 1c, 1g).



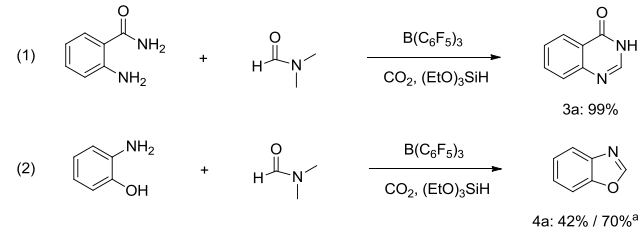
Scheme 1. Synthesis of various benzothiazoles. Reaction conditions: Reactant (0.5 mmol), $B(C_6F_5)_3$ (5 mol%), Et_2SiH_2 (2.5 mmol), DMF (1 mL), CO_2 (0.1 MPa), 120 °C, 24 h; [a]Reaction time: 40 h. The yields were determined by ^1H NMR (DMSO-d_6, 400 MHz) using pyrazine as an internal standard. Isolated yields were in the bracket.

Encouraged by the great success in the reactions of 2-aminothiophenols with DMF to various benzothiazoles, we applied $B(C_6F_5)_3$ in catalysing the cycloaddition of diverse *o*-phenylenediamines with DMF. Using Et_2SiH_2 as the silane, benzimidazole was obtained in a poor yield of 15% under atmospheric CO_2 pressure at 120 °C for 24 h, while triethoxysilane ($(EtO)_3SiH$) afforded a product yield of 99% under the same other conditions. Hence, $(EtO)_3SiH$ instead of Et_2SiH_2 was used in the cyclization of *o*-phenylenediamines with DMF. As shown in Scheme 2, $B(C_6F_5)_3$ combined with atmospheric CO_2 was very effective for catalysing DMF to react with all the tested *o*-phenylenediamines, affording the corresponding products in excellent yields in most cases. For example, substituents on phenyl ring of diamines with disparate electronic properties had no obvious bias on the formation of products (Scheme 2, 2a-k). Ortho- and bis-substituents on the benzene moiety showed no obvious influence on the reaction outcome (Scheme 2, 2c-d, 2h). It was noteworthy that both ester and ketone functionalities remained intact after reaction, which was important for the production of these kinds of benzimidazoles (Scheme 2, 2l-n). In addition, the N-methyl and phenyl substituted diamines could give rise to 2o and 2p smoothly despite the increased steric hindrance for the cyclization. As examples of diamines containing N-heteroatoms, 2,3- and 3,4-diaminopyridine were also amenable to this protocol (Scheme 2, 2q-r). Interestingly, *o*-phenylenediamine containing an extended conjugated system could proceed successfully as well, and the corresponding product 2s was obtained in a yield of 94%.



Scheme 2. Synthesis of benzimidazoles. Reaction conditions: Reactant (0.5 mmol), $B(C_6F_5)_3$ (5 mol%), $(EtO)_3SiH$ (5 mmol), DMF (1 mL), CO_2 (0.1 MPa), 120 °C, 24 h. The Yields were determined by ^1H NMR (DMSO-d_6, 400 MHz) using pyrazine as an internal standard. Isolated yields were in the bracket.

Inspired by the above results, we further explored the cyclization of less reactive but more challenging substrates with DMF catalysed by $B(C_6F_5)_3$ in the presence of CO_2. To our delight, anthranilamide bearing an amide group gave rise to 4-quinazolinone in a yield of 99% despite the less-nucleophilic ability of the amide group for the condensation step (Scheme 3, equation 1). In addition, the inert substrate 2-aminophenol could also be cyclized with DMF, producing 4a in a yield of 42%. As the CO_2 pressure was increased to 1 MPa, benzoxazole was obtained in a yield of 70% (Scheme 3, equation 2). These findings indicated that the $B(C_6F_5)_3$-CO_2 catalytic system was highly efficient for the synthesis of N-containing heterocycles.



Scheme 3. Synthesis of quinazolinone and benzoxazole. Reaction conditions: Reactant (0.5 mmol), $B(C_6F_5)_3$ (5 mol%), $(EtO)_3SiH$ (5 mmol), DMF (1 mL), CO_2 (0.1 MPa), 120 °C, 24 h. The Yields were determined by ^1H NMR (DMSO-d_6, 400 MHz) using pyrazine as an internal standard. [a]CO_2 pressure was 1 MPa.

To explore the possible reaction mechanism, a series of experiments were conducted. First, the interaction of $B(C_6F_5)_3$

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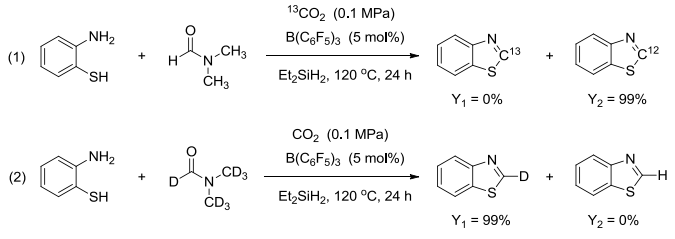
with DMF was examined by ^{1}H, ^{13}C, ^{11}B and ^{19}F NMR analyses, as shown in Figure S1. From the ^{1}H NMR spectra of DMF and its mixture with $B(C_6F_5)_3$, it was found that the signals of H atoms from CH_3 (1, 2) and CHO (3) of DMF in the mixture shifted downfield from δ 2.14 to 2.68, δ 2.45 to 2.71 and δ 7.74 to 8.37, respectively; meanwhile, the signals of C atoms from CH_3 (1, 2) and CHO (3) of DMF in the mixture shifted downfield from δ 30.30 to 34.17, δ 34.92 to 38.74 and δ 161.51 to 165.55, respectively. Moreover, the B atom in $B(C_6F_5)_3$ showed an upfield shift from δ 14.64 to -0.36 after interaction with DMF. The ^{19}F NMR signals assigning to F (1, 2, 3) atoms in $B(C_6F_5)_3$ shifted upfield from -160.35, -144.30, -128.92 ppm to -162.22, -155.10, -133.01 ppm, respectively , as $B(C_6F_5)_3$ mixed with DMF. All these shifts demonstrated the strong electrostatic interaction between DMF and $B(C_6F_5)_3$, suggesting that DMF was activated by $B(C_6F_5)_3$. The C-N bond of DMF was weaken, making it more favorable to break, thus easily releasing the -CHO building block for reaction.[15]

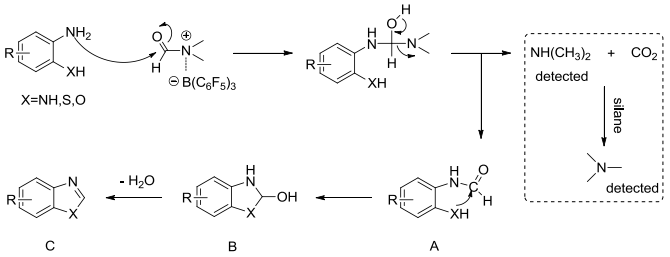
The cyclization of 2-aminothiophenol with DMF in the presence of atmospheric CO_2 and Et_2SiH_2 catalyzed by $B(C_6F_5)_3$ was conducted at 120°C for 15h, and the reaction solution was examined by GC-MS analysis. A new small peak appeared at t = 1.333 s with the molecular ion (M+) peak of 45 (Figure S2), attributing to dimethylamine (m/z=45), which suggested that DMF reacted with 2-aminothiophenol to form a formylated intermediate and release dimethylamine as the leaving group of DMF. Another small peak appeared at t=1.325 s (see Figure S2), assigning to trimethylamine, implying that the intermediate dimethylamine further reacted with CO_2 and silane catalyzed by $B(C_6F_5)_3$, forming trimethylamine, which drove the cyclization reaction to the right, thus greatly promoting the reaction.

To further probe the role of CO_2 in this cyclization reaction, isotope-labeling experiments were performed, as shown in Scheme 4. Using $^{13}CO_2$, ^{13}C-labelled benzothiazole was not detected, while non-labelled product was obtained in 99% yield. Using [D_7]-DMF instead of DMF, D-labelled benzothiazole was obtained in 99% yield. From these results, it can be concluded that DMF served as the formylation reagent, while CO_2 was a promoter to drive the reaction to the right.



Scheme 4. Isotope-labeling experiments.

On the basis of the experimental results and previous reports,[5, 14-16] a possible mechanism was proposed, as shown in Scheme 5. Firstly, DMF was activated by $B(C_6F_5)_3$ via electrostatic interaction, thus making the nucleophilic attack of substrates much easier to form formylated intermediate A. Simultaneously, dimethylamine was released as the leaving group of DMF, which may further react with CO_2 and silane to form the trimethylamine product and drove the reaction to the right, thus greatly promoting the reaction. Then the intramolecular nucleophilic cyclization of A and dehydration reaction of B took place successively, thus yielding product C.



Scheme 5. Possible reaction pathway.

4. Conclusions

In summary, $B(C_6F_5)_3$ combined with atmospheric CO_2 was found to be highly effective for the cyclization of various kinds of ortho-substituted aniline derivatives with DMF, and a series of N-containing heterocycles including benzothiazoles, benzomidazoles, quinazolinone and benzoxazole were obtained in good to excellent yields. This work presented a new metal-free catalytic system for the production of N-containing heterocyclic compounds, also opened a new way for the utilization of CO_2 in green chemical processes.

Acknowledgements

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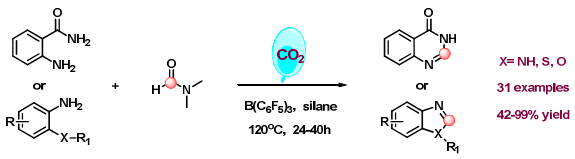
Graphic Abstract



CO_2 gas greatly promoted the cyclization of various o-substituted anilines with N,N-dimethylformamide, producing N-containing heterocycles in high yields.