Heteroatom Chemistry
Volume 5, Number 5/6, 1994

Convenient Synthesis of Heterocycles by Sulfur-Assisted Carbonylation at Ordinary Pressure and Temperature

Takumi Mizuno,* Hitoshi Toba, Toshiyuki Miyata, and Ikuzo Nishiguchi

Osaka Municipal Technical Research Institute, 1-6-50, Morinomiya, Joto-ku Osaka 536, Japan

Received 26 May 1994; revised 19 July 1994

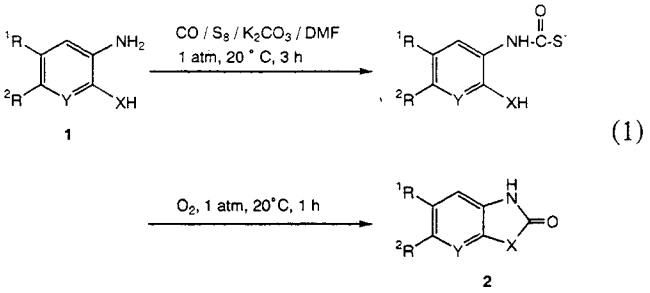
ABSTRACT

Heterocyclic compounds, including benzimidazolones, naphthimidazolone, benzoxazolones, benzothiazolone, quinazolinone, benzoxazinone, quinazolinedione, and imidazopyridinone were synthesized in good yields by sulfur-assisted carbonylation of aromatic amines with carbon monoxide (1 atm) at room temperature, with subsequent oxidation using molecular oxygen (1 atm, RT). The present method is characterized as a simple procedure carried out under quite mild conditions.

INTRODUCTION

Elemental sulfur promotes carbonylation of amines with carbon monoxide to form urea derivatives [1–3] and thiocarbamates [4]. However, these reactions have been carried out under drastic conditions (high pressure and temperature). Very recently, we developed a convenient synthesis of urea derivatives by the combination of the sulfur-assisted carbonylation of primary amines using carbon monoxide, with a subsequent oxidation of formed ammonium salts of thiocarbamates using molecular oxygen under mild conditions such as ordinary pressure and room temperature [5].

Herein, we wish to report a facile synthesis of a variety of nitrogen-containing heterocycles [6,8] from aromatic amines using sulfur-assisted carbonylation with carbon monoxide at atmospheric pressure and subsequent oxidation with molecular oxygen (1 atm) at room temperature (Equation 1).



1 (1) 2

RESULTS AND DISCUSSION

At the outset, the effects of several bases were examined on the synthesis of benzimidazolone (**2a**) from 1,2-diaminobenzene (**1a**) (Table 1). It was found that the use of a base is essential for this sulfur-assisted carbonylation and that the character of the base has a remarkable influence on the yield of **2a**. Among the bases, the use of potassium carbonate (72%) or of *N*-methylpyrrolidine (75%) gave relatively good results.

A variety of heterocyclic compounds (benzimidazolones, naphthimidazolone, benzoxazolones, benzothiazolone, quinazolinone, benzoxazinone, quinazolinedione, and imidazopyridinone) (**2a–l**) were prepared by the herein described sulfur-assisted carbonylation of aromatic amines with carbon monoxide in the presence of potassium carbonate (which is easily available and manipulable) for 3 hours at ordinary pressure and temperature,

*To whom correspondence should be addressed.

1042-7163/94/$5.00 + .25

TABLE 1 Effect of Bases for Synthesis of Benzimidazolone (**2a**)

Base	*Yield, %*[a]	*Base*	*Yield, %*[a]
K_2CO_3	72	DBU	57
K_2CO_3[b]	0	DABCO	32
NaOH	52		75
None	0	Et_3N	51

[a]Isolated yields based on 1,2-diaminobenzene used.
[b]Carbonylation was performed under a nitrogen atmosphere.

TABLE 2 Synthesis of Heterocycles (**2a–l**)

Entry	*R*[1]	*R*[2]	*X*	*Y*		*Yield, %*[a]
1	H	H	NH	CH	**2a**	72
2	CH_3	H	NH	CH	**2b**	78
3	CH_3	CH_3	NH	CH	**2c**	93
4	Cl	H	NH	CH	**2d**	100
5	$-(CH=CH)_2-$		NH	CH	**2e**	76
6	H	H	O	CH	**2f**	84
7	CH_3	H	O	CH	**2g**	67
8	H	H	S	CH	**2h**	99
9	H	H	CH_2NH	CH	**2i**	34
10	H	H	CH_2O	CH	**2j**	44
11	H	H	C(O)NH	CH	**2k**	51[b]
12	H	H	NH	N	**2l**	37

[a]Yield of pure isolated product.
[b]In place of K_2CO_3, DBU was used as a base.

with subsequent oxidation with molecular oxygen for 1 hour under similar mild conditions (Table 2).

Generally, benzimidazolones, naphthimidazolone, benzoxazolones, and benzothiazolone (**2a–h**) were easily isolated as pure products by simple purification (short column chromatography or recrystallization) in good to excellent yields (entries 1–8). Quinazolinone, benzoxazinone, and imidazopyridinone (**2i**, **2j**, and **2l**) were also successfully obtained, although the yields of these products were unsatisfactory (entries 9, 10, and 12). Synthesis of quinazolinedione (**2k**) from 2-aminobenzamide (**1k**) in moderate yield could be effected in the presence of DBU instead of potassium carbonate (entry 11).

The following scheme shows a plausible pathway for the present synthesis of heterocycles **2** under mild conditions. Elemental sulfur reacts with carbon monoxide to give carbonyl sulfide (**3**) *in situ* [18]. Generated **3** reacts with the aromatic amines to form the salts of thiocarbamates **4**. Oxidation of **4** with molecular oxygen may lead to formation of biscarbamoyl disulfides **5** as intermediates [20,21], which are subjected to aminolysis to give heterocycles **2**.

Because of the usefulness of the products, mild conditions (no need of an autoclave and heating or cooling), good yields, practical simplicity, and the use of easily available reagents, the present method

SCHEME 1

may provide a useful route for synthesis of benzoheterocyclic compounds 2, even on a large scale, starting from aromatic amines, carbon monoxide, elemental sulfur, and molecular oxygen.

EXPERIMENTAL

General

Melting points were determined on a Mettler FP 5 apparatus and were uncorrected. Infrared (IR) spectra were recorded on a Shimadzu IR-435 spectrometer ^1H and ^{13}C NMR spectra were obtained on a JEOL JNM-EX270 (270 MHz) instrument. Chemical shifts were reported as δ values relative to tetramethylsilane. Mass and exact mass spectra were recorded on a JEOL JMS-DX303HF spectrometer. DMF was purified by distillation. Aromatic amines, powdered sulfur (99.5%), potassium carbonate (99.5%), carbon monoxide (99.9%), and oxygen (99.5%) were used as purchased.

Typical Procedure for Synthesis of Benzoxazolone (**2f**)

Elemental sulfur (0.64 g, 20 mmol) and potassium carbonate (4.15 g, 30 mmol) were added to a DMF solution (20 mL) of 2-hydroxyaniline (**1f**) (1.09 g, 10 mmol), and the solution was vigorously stirred at 20°C for 3 hours under atmospheric pressure of one atmosphere of carbon monoxide. After evacuation of carbon monoxide, oxidation of the resulting mixture with molecular oxygen (1 atm) was performed at 20°C with stirring for 1 hour [23]. Then, the resulting solution was poured into cooled 1N HCl (200 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The extract was dried over $MgSO_4$ and the solvent was removed. Purification by short-col-

umn chromatography (silica gel, AcOEt) gave benzoxazolone (**2f**) in 84% yield (1.13 g), based on **1f**.

Benzimidazolone (**2a**). Mp >300°C (Ref. [12], 311°C); IR (KBr) 3100, 3000, 1720, 730 cm^{-1}; ^1H NMR (d_6 DMSO) δ 6.93 (s, 4H), 10.58 (brs, 2H); ^{13}C NMR (d_6 DMSO) δ 108.4, 120.3, 129.5, 155.2; MS, *m/z*, 134 (M^+); exact MS calcd. for $C_7H_6N_2O$ 134.0480; found: 134.0486.

5-Methylbenzimidazolone (**2b**). Mp >300°C (Ref. [12], 293–295°C); IR (KBr) 3100, 1740, 780 cm^{-1}; ^1H NMR (d_6 DMSO) δ 2.27 (s, 3H), 6.71–6.82 (m, 3H), 10.44 (brs, 1H), 10.47 (brs, 1H); ^{13}C NMR (d_6 DMSO) δ 21.0, 108.1, 109.0, 120.8, 127.4, 129.3, 129.8, 155.4; MS, *m/z*, 148 (M^+); exact MS calcd. for $C_8H_8N_2O$ 148.0637; found: 148.0664.

5,6-Dimethylbenzimidazolone (**2c**) [*24*]. Mp >300°C (Ref. [13], 384–386°C); IR (KBr) 3100, 2950, 1680, 1490 cm^{-1}; MS, *m/z*, 162 (M^+); exact MS calcd. for $C_9H_{10}N_2O$ 162.0793; found: 162.0792.

5-Chlorobenzimidazolone (**2d**). Mp >300°C (Ref. [13], 324–326°C); IR (KBr) 3150, 3000, 1750, 790 cm^{-1}; ^1H NMR (d_6 DMSO) δ 6.90–6.97 (m, 3H), 10.78 (brs, 2H); ^{13}C NMR (d_6 DMSO) δ 108.4, 109.5, 120.0, 124.5, 128.6, 130.8, 155.2; MS, *m/z*, 168 (M^+); exact MS calcd. for $C_7H_5ClN_2O$ 168.0090; found: 168.0100.

Naphthimidazolone (*1H-naphth[2,3-d]imidazol-2(3H)-one*) (**2e**). Mp >300°C (Ref. [12], >320°C); IR (KBr) 3100, 3050, 1750, 840, 730 cm^{-1}; ^1H NMR (d_6 DMSO) δ 7.28–7.33 (m, 4H), 7.79–7.84 (m, 2H), 10.82 (brs, 2H); ^{13}C NMR (d_6 DMSO) δ 103.6, 123.2, 126.8, 129.2, 131.1, 156.2; MS, *m/z*, 184 (M^+); exact MS calcd. for $C_{11}H_8N_2O$ 184.0637; found: 184.0658.

Benzoxazolone (**2f**). Mp 140.0°C (Ref. [9], 139–140°C); IR (KBr) 3250, 1770, 1730, 1480 cm^{-1}; ^1H NMR (d_6 DMSO) δ 7.05–7.18 (m, 3H), 7.26–7.29 (m, 1H), 11.61 (brs, 1H); ^{13}C NMR (d_6 DMSO) δ 109.5, 109.7, 121.8, 123.7, 130.3, 143.3, 154.4; MS *m/z*, 135 (M^+); exact MS calcd. for $C_7H_5NO_2$ 135.0320; found: 135.0292.

5-Methylbenzoxazolone (**2g**). Mp 128.4°C (Ref. [9], 128–129°C); IR (KBr) 3250, 1780, 1730, 1260 cm^{-1}; ^1H NMR (d_6 DMSO) δ 2.31 (s, 3H), 6.87 (d, 1H, J = 8), 6.89 (s, 1H), 7.13 (d, 1H, J = 8), 11.49 (brs, 1H); ^{13}C NMR (d_6 DMSO) δ 109.0, 110.0, 122.0, 130.2, 133.1, 141.3, 154.6; MS, *m/z*, 149 (M^+); exact MS calcd. for $C_8H_7NO_2$ 149.0477; found: 149.0495.

Benzothiazolone (**2h**). Mp 135.5°C (Ref. [25], 138°C); IR (KBr) 3100, 3050, 1650, 1460 cm^{-1}; ^1H NMR (d_6 DMSO) δ 7.10–7.15 (m, 2H), 7.25–7.31 (m, 1H), 7.54–7.57 (m, 1H), 11.86 (brs, 1H); ^{13}C NMR (d_6 DMSO) δ 111.4, 122.5, 122.6, 123.3, 126.3, 136.6, 170.0; MS, *m/z*, 151 (M^+); exact MS calcd. for C_7H_5NOS 151.0092; found: 151.0081.

Quinazolinone (*3,4-dihydro-2(1H)-quinazolinone*) (**2i**). Mp 232.8°C (Ref. [26], 229–231°C); IR (KBr) 3250, 1720, 1490, 740 cm^{-1}; ^1H NMR (d_6 DMSO) δ 4.30 (s, 2H), 6.75–6.87 (m, 3H), 7.04–7.12 (m, 2H), 8.99 (brs, 1H); ^{13}C NMR (d_6 DMSO) δ 42.8, 113.8, 118.4, 121.2, 125.9, 127.8, 138.4, 154.9; MS, *m/z*, 148 (M^+); exact MS calcd. for $C_8H_8N_2O$ 148.0637; found: 148.0658.

Benzoxazinone (*1,4-dihydro-(2H)-3,1-benzoxazin-2-one*) (**2j**). Mp 118.2°C (Ref. [7], 118.5–119°C); IR (KBr) 3100, 1710, 1600 cm^{-1}; ^1H NMR (d_6 DMSO) δ 5.27 (s, 2H), 6.87–7.03 (m, 2H), 7.18–7.27 (m, 2H), 10.13 (brs, 1H); ^{13}C NMR (d_6 DMSO) δ 67.4, 113.5, 118.5, 122.2, 124.3, 128.2, 136.4, 151.7; MS, *m/z*, 149 (M^+); exact MS calcd. for $C_8H_7NO_2$ 149.0477; found: 149.0502.

Quinazolinedione (*2,4(1H,3H)-quinazolinedione*) (**2k**). Mp >300°C (Ref. [27], >300°C); IR (KBr) 3250, 3050, 1700, 1660, 1440 cm^{-1}; ^1H NMR (d_6 DMSO) δ 7.16–7.21 (m, 2H), 7.61–7.67 (m, 1H), 7.88–7.91 (m, 1H), 11.13 (brs, 1H), 11.26 (brs, 1H); ^{13}C NMR (d_6 DMSO) δ 114.3, 115.3, 122.3, 126.9, 134.9, 140.8, 150.2, 162.8; MS, *m/z*, 162 (M^+); exact MS calcd. for $C_8H_6N_2O_2$ 162.0429; found: 162.0451.

Imidazopyridinone (*1H-imidazo[4,5-b]pyridin-2(3H)-one*) (**2l**). Mp 273.0°C (Ref. [7], 272–273°C); IR (KBr) 3450, 2950, 2800, 1670, 1415, 760 cm^{-1}; ^1H NMR (d_6 DMSO) δ 6.94 (dd, 1H, J = 5, 7), 7.22 (d, 1H, J = 7), 7.87 (d, 1H, J = 5), 10.81 (brs, 1H), 11.28 (brs, 1H); ^{13}C NMR (d_6 DMSO) δ 114.2, 116.5, 123.6, 139.5, 144.7, 154.4; MS, *m/z*, 135 (M^+); exact MS calcd. for $C_6H_5N_3O$ 135.0433; found: 135.0417.

ACKNOWLEDGMENT

This work was supported by a Grant-in Aid for Scientific Research on Priority Area No. 05235107 from the Ministry of Education, Science and Culture, Japan.

REFERENCES

[1] R. A. Franz, F. Applegath, *J. Org. Chem.*, *26*, 1961, 3304.
[2] R. A. Franz, F. Applegath, F. V. Morriss, F. Baiocchi, *J. Org. Chem.*, *26*, 1961, 3306.
[3] R. A. Franz, F. Applegath, F. V. Morriss, F. Baiocchi, C. Bolze, *J. Org. Chem.*, *26*, 1961, 3309.
[4] D. W. Grisley, Jr., J. A. Stephens, *J. Org. Chem.*, *26*, 1961, 3568.
[5] T. Mizuno, M. Matsumoto, I. Nishiguchi, T. Hirashima, *Heteroatom Chem.*, *4*, 1993, 455.
[6] These heterocycles are used as important precursors of pigments, resins, and bioactive compounds [7].

[7] T. Yoshida, N. Kambe, S. Murai, N. Sonoda, *Bull. Chem. Soc. Jpn., 60*, 1987, 1793.
[8] These heterocycles are generally prepared by the carbonylation of aromatic amines with phosgene and urea as carbonyl sources [9–11]. Other synthetic methods were also reported using carbonylation with carbonyldiimidazole [12,13], carbon monoxide in the presence of selenium-catalyst [7,14,15], and reductive carbonylation with carbon monoxide, elemental sulfur, and water [16,17].
[9] W. J. Close, B. D. Tiffany, M. A. Spielman, *J. Am. Chem. Soc., 71*, 1949, 1265.
[10] R. L. Clark, A. A. Pessolano, *J. Am. Chem. Soc., 80*, 1958, 1657.
[11] R. L. Clark, A. A. Pessolano, *J. Am. Chem. Soc., 80*, 1958, 1662.
[12] H. A. Staab, *Liebigs Ann. Chem., 609*, 1957, 75.
[13] W. B. Wright, Jr., *J. Heterocyclic Chem., 2*, 1965, 41.
[14] N. Sonoda, G. Yamamoto, K. Natsukawa, K. Kondo, S. Murai, *Tetrahedron Lett.*, 1975, 1969.
[15] T. Yoshida, N. Kambe, S. Murai, N. Sonoda, *Tetrahedron Lett., 27*, 1986, 3037.
[16] K. Konishi, I. Nishiguchi, T. Hirashima, N. Sonoda, S. Murai, *Synthesis*, 1984, 254.
[17] T. Miyata, N. Kambe, S. Murai, N. Sonoda, I. Nishiguchi, T. Hirashima, *J. Chem. Soc. Jpn.*, 1987, 1332.
[18] Carbonyl sulfide was synthesized from carbon monoxide, elemental sulfur, and secondary amines [19].
[19] E. A. Swakon: U.S. 3382043 (1968), Standard Oil Co.: *Chem. Abstr. 68* (1968) 116058.
[20] Bis(*N*-methyl-*N*-phenylcarbamoyl) disulfide (35%) was prepared by oxidation of lithium *N*-methyl-*N*-phenylthiocarbamate with iodine at 0°C.
[21] In the reaction system of selenium-catalyzed carbonylation of primary amines with carbon monoxide to give urea derivatives, the formation of biscarbamoyl diselenides as intermediates was proposed [22].
[22] S. Fujiwara, N. Miyoshi, A. Ogawa, N. Kambe, N. Sonoda, *J. Phys. Org. Chem., 2*, 1989, 359.
[23] The mixture was cooled by use of a water bath, if necessary, because this oxidation was sometimes exothermic.
[24] ^{1}H NMR and ^{13}C NMR could not be measured because of insolubility of ***2c***. However, this compound afforded spectral data (IR, MS) in complete accordance with those of an authentic sample [13].
[25] R. F. Hunter, *J. Chem. Soc.*, 1930, 125.
[26] G. Kempter, H. J. Ziegner, G. Moser, W. Natho, *Wiss. Z. Paedagog. Hochsch. "Karl Liebknecht" Potsdam, 21*, 1977, 5: *Chem. Abstr. 89* (1978) 163560.
[27] T. Miyata, T. Mizuno, Y. Nagahama, I. Nishiguchi, T. Hirashima, N. Sonoda, *Heteroatom Chem., 2*, 1991, 473.