Iranian Journal of Organic Chemistry Vol. 12, No.2 (2020) 2861-2865

IranJOC
Iranian Journal of Organic Chemistry

Synthesis of 1,3-oxazole using the reaction of aziridine with CO_2 under solvent-free condition

Sayyed Jalal Shams-Najafi[a*] and Faramarz Rostami-Charati[b]

[a]*Department of Chemistry,Faculty of Sciences, Ferdowsi University of Mashhad, Mashhad 91779-1436, I.R. Iran*
[b]*Research Center for Conservation of Culture Relicst (RCCCR), Research institute of Cultural Heritage &Tourism, Tehran, Iran.*

Received: February 2020; Revised: February 2020; Accepted: April 2020

Abstract: An efficient one-pot synthesis of functionalized 1,3-oxazole-2-ones is described via reaction of carbon dioxide with aziridines in the presence of sodium hydride (10 mol%)/MeOH.

Keywords: Oxazole; Aziridine; Carbon dioxide; Sodium hydride; Methoxide ion.

Introduction

Multicomponent reactions (MCRs), with three or more reactants join in a one-pot procedure to afford a single product [1-3]. They are economically and environmentally useful because multi-step synthesis produce large amounts of trash frequently because of complex isolation actions frequently involving comfortable, toxic, and hazardous solvents after each step [4-7]. MCRs are absolutely suited for combinatorial library synthesis and increased utilize in the finding procedure for new drugs and agrochemicals [8]. They supply a dominant tool toward the one-pot synthesis of diverse and complex compounds as well as small and drug-like heterocycles [9]. Green chemistry move towards hold out significant potential not only for reduction of byproducts, waste produced, and lowering of energy but also in the expansion of new methodologies toward before exclusive materials, using existing technologies [10]. Between existing part of chemistry, medicinal and pharmaceutical chemistry are possibly developed for greening [11].

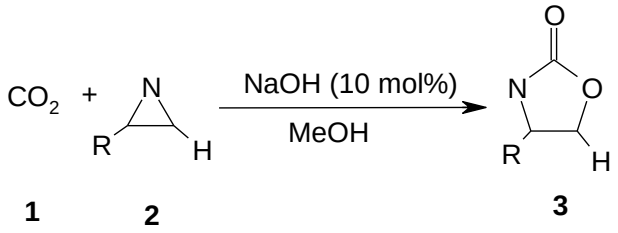
*Corresponding author: Tel: 0098-8633677201-9; Fax: 0098-8633677203, E-mail: sj.shamsnajafi7148@gmail.com

It should be mentioned, heterocyclic compounds are a highly valuable and unique class of compounds. These compounds demonstrate a broad spectrum of physical, chemical and biological characteristics [12, 13]. In nature, heterocyclic compounds are widely distributed and display an important part in metabolism owing to their structural nucleus occurring in various natural products, including hormones, antibiotics, alkaloids, vitamins and many others [14, 15]. Among heterocyclic compounds, nitrogen-containing heterocycles are considerably found as a main structure in a enormous library of heterocycles and display several employments in natural science and other areas of science [16]. As well, nitrogen-containing heterocycles are broadly displayed in natural products, for instance, vitamins, hormones and alkaloids [17, 18]. Among them, oxazole derivatives demonstrate a broad spectrum of biological activities such as anti-tubercular [19], anti-AIDS [20], anti-malarial [21], anti-microbial [22], antitumor [23, 24], anticancer [25] and antifungal [26]. In addition, oxazoles have also been found as promising anti-hyperglycemic [27], anti-depressant [28], anti-convulsant [29], anti-pyretic [30], anti-anxiety [31, 32] and insecticidal agents [33].

Results and discussion

Our studies were initiated by treating a solution of carbon dioxide containing an aziridine derivatives in the presence of sodium hydroxide (10 mol%). The efficiency of this reaction was low because hydroxide ion is weak leaving group (Scheme **1**). Our studies were initiated by treating a solution of carbon disulfide containing an oxirane derivative in the presence of sodium hydroxide (10 mol%). The efficiency of this reaction was low because hydroxide ion is weak leaving group.

The nucleophile derived from methanol and carbon disulfide in the presence of sodium hydride (10 mol%) was found to undergo a clean and facile reaction with oxiranes at room temperature to afford 2 in excellent yields (Scheme **2**).

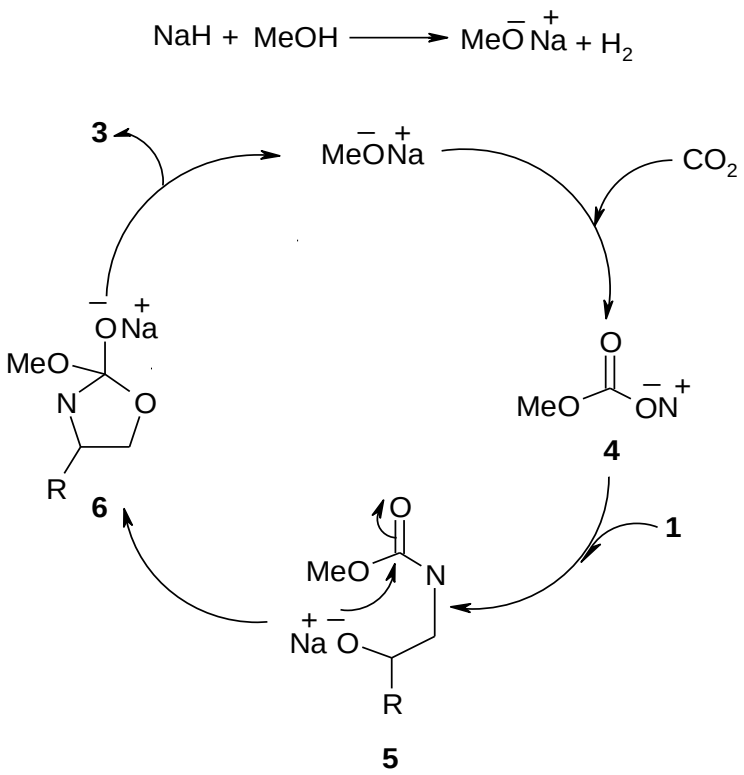


1 **2** **3**

1, 3	R	R'	Yield (%) of **3**
a	Me	H	96
b	Et	H	94
c	R, R' = $(CH_2)_4$		96
d	Ph	H	95
e	$PhOCH_2$	H	94
f	$CH_2CHCH_2OCH_2$	H	94
g	$(CH_3)_2CHOCH_2$	H	96
h	Ph	Ph(*cis*)	88
i	Ph	Ph(*trans*)	86

Scheme 1: Synthesis of oxazole **3**

Structures of compounds **3a–3i** were confirmed by IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data. For example, the ^{1}H NMR spectrum of **3a** exhibited a triplet at 1.56 (^3J = 6.7) for the methyl proton, two doublet doublets at 3.62 (2J = 11.9, ^3J = 7.4) and 3.98 (^2J = 11.9, ^3J = 6.4) for the CH_2 moiety and a multiplet at 4.45-4.51 ppm for the CH group. The ^{13}C NMR spectrum of **3a** shows a signal at 228.5 ppm for the C=O group. The mass spectrum of 3a displayed the molecular ion peak at m/z = 145. A tentative mechanism for this transformation is proposed in Scheme **2**. The first step may involve addition of methoxide ion to CO2 and formations of the 1:1 adduct 3. Subsequent nucleophilic attack of 4 to 1 yields 5, which is converted to **3** by elimination of sodium methoxide.



Scheme 2: Proposed mechanism for the formation of **3**.

Conclusion

In conclusion, the reaction of methanol and carbon dioxide with aziridine in the presence of sodium hydride (10 mol%) led to 1,3-oxazoles in excellent yields.

Experimental

General.

Melting points were measured on an *Electrothermal 9100* aparatus. further purification. IR Spectra: *Shimadzu IR-460* spectrometer. ^{1}H-and ^{13}C-NMR spectra: *Bruker DRX-500 AVANCE* instrument; in $CDCl_3$ at 500.1 and 125.7 MHz, resp; δ in ppm, *j* in Hz. EI-MS (70 eV): *Finnigan-MAT-8430* mass spectrometer, in m/z. Elemental analyses (C, H, N) were performed with a *Heraeus CHN-O-Rapid* analyzer.

General Procedure for the Preparation of Compounds **2.**

To a stirred solution of CS_2 (0.35 g, 5 mmol) in MeOH (0.064 g, 2 mmol) containing NaH (10 mol%), was added the oxirane derivative **1** (2 mmol) at r.t. The mixture was stirred for 12 h, and filtered to remove NaOMe. The residue was purified by extraction with Et_2O to afford pure **2**.

5-Methyl-1,3-oxazole-2-one (3a):

Yellow oil, yield: 0.26 g (96%). IR (KBr) (ν_{max}/cm^{-1}): 1700, 1439, 1414, 1370, 1143, and 1073 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.56 (3 H, *d*, ^{3}J = 6.7, Me), 3.62 (1 H, *dd*, ^{2}J = 11.9, ^{3}J = 7.4, CH), 3.98 (1 H, *dd*, ^{2}J = 11.9, ^{3}J = 6.4, CH), 4.45-4.51 (1H, *m*, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 19.1 (Me), 50.3 (CH_2), 55.5 (CH), 228.5 (C=S). EI-MS: EI-MS: 134 (M^+, 15), 119 (78), 92 (100), 76 (64), 58 (48), 42 (56). Anal. Calcd for $C_4H_6OS_2$ (134.21): C, 35.80; H, 4.51; found: C, 35.90; H, 4.55%.

5-Ethyl-1,3-oxazole-2-one (3b):

Yellow oil, yield: 0.28 g (94%). IR (KBr) (ν_{max}/cm^{-1}): 1711, 1627, 1507, 1431, 1327, and 1273 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.07 (3 H, *t*, ^{3}J = 7.4, Me), 1.91-1.97 (2 H, *m*, CH_2), 3.71 (1 H, *dd*, ^{2}J = 11.9, ^{3}J = 7.5, CH), 3.98 (1 H, *dd*, ^{2}J = 11.9, ^{3}J = 5.5, CH),

4.29-4.33 (1 H, *m*, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 13.1 (Me), 27.2 (CH_2), 48.3 (CH_2), 62.9 (CH), 228.5 (C=S). EI-MS: 148 (M^+, 10), 119 (68), 92 (100), 76 (84), 56 (42), 29 (24). Anal. Calcd for $C_5H_8OS_2$ (148.24): C, 40.51; H, 5.44; found: C, 40.41; H, 5.49%.

Hexahydro-1,3-benzoxazole-2-one (3c):

Yellow crystals, yield: 0.33 g (96%); mp 176-178°C. IR (KBr) (ν_{max}/cm^{-1}): 1628, 1431, 1326, 1272, and 1094 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.43-1.48 (2 H, *m*, CH_2), 1.68-1.75 (2 H, *m*, CH_2), 1.93-1.97 (2 H, *m*, CH_2), 2.17-2.22 (2 H, *m*, CH_2), 4.08-4.09 (1 H, *m*, CH), 4.09-4.11 (1 H, *m*, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$); δ 25.5 (2 CH_2), 29.5 (2 CH_2), 65.0 (2 CH), 227.6 (C=S). EI-MS: 174 (M^+, 5), 118 (78), 92 (100), 82 (64), 76 (48), 56 (45). Anal. Calcd for $C_7H_{10}OS_2$ (174.27): C, 48.24; H, 5.78; found: C, 48.18; H, 5.79%.

5-Phenyl-1,3-oxazole-2-one (3d):

Yellow crystals, yield: 0.30 g (95%); mp 115-117°C. IR (KBr) (ν_{max}/cm^{-1}): 1568, 1470, 1438, 1413, 1357, and 1048 cm^{-1}; ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 4.03 (1 H, *dd*, ^2J = 12.0, ^3J = 5.7, CH), 4.17 (1 H, *dd*, ^2J =12.0, ^3J = 11.8, CH), 5.65 (1 H, *dd*, ^2J = 10.3, ^3J = 5.7, CH), 7.37-7.44 (3 H, *m*, 3 CH), 7.50 (2 H, *d*, ^3J = 7.2, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 49.8 (CH_2), 64.2 (CH), 127.5 (2 CH), 129.2 (2 CH), 129.3 (CH), 135.3 (C), 227.2 (C=S). EI-MS: 196 (M^+, 10), 119 (76), 104 (46), 92 (25), 77 (100). Anal. Calcd for $C_9H_8OS_2$ (196.28): C, 55.07; H, 4.11; found: C, 55.03; H, 4.08%.

5-(Phenoxymethyl)-1,3-oxazole-2-one (3e):

Yellow crystals, yield: 0.42 g (94%); mp 55-57°C. IR (KBr) (ν_{max}/cm^{-1}): 1584, 1481, 1448, 1238, 1165, and 1063 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 4.06 (1 H, *dd*, ^2J = 12.3, ^3J = 4.0, CH), 4.18-4.23 (2 H, *m*, CH_2), 4.36 (1 H, *dd*, ^2J = 12.2, ^3J = 4.5, CH), 4.61-4.66 (1 H, *m*, CH), 6.93 (2 H, *d*, ^3J = 7.9, 2 CH), 7.02 (1 H, *t*, ^3J = 7.3, CH), 7.33 (2 H, *t*, ^3J = 7.5, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 45.0 (CH_2), 57.4 (CH), 66.7 (CH), 114.7 (2 CH), 121.9 (CH), 129.7 (2 CH), 157.8 (C), 225.4 (C=S). EI-MS: 226 (M^+, 5), 149 (78), 134 (64), 107 (94), 92 (46), 77 (100). Anal. Calcd for $C_{10}H_{10}O_2S_2$ (226.31): C, 53.07; H, 4.45; found: C, 53.05; H, 4.40%.

5-(Vinyloxymethyl)-1,3-oxazole-2-one (3f):

Yellow oil, yield :0.36 g (94%). IR (KBr) (ν_{max}/cm^{-1}): 1702, 1630, 1451, 1414, and 1348 cm-1. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 3.64 (1 H, *dd*, ^2J = 9.8, ^3J = 5.8, CH), 3.79-3.81 (1 H, *m*, CH), 3.94 (1 H, *dd*, ^2J = 12.1, ^3J = 4.7, CH), 4.04 (2 H, *d*, ^3J = 5.6, 2 CH), 4.07 (1 H, *dd*, ^2J = 12.1, ^3J = 5.7, CH), 4.44-4.49 (1 H, *m*, CH), 5.20-5.30 (2 H, *m*, 2 CH), 5.83-5.91(1 H, *m*, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 45.4 (CH_2), 58.7 (CH), 69.4 (CH_2), 72.8 (CH_2), 118.4 (CH_2), 134.3 (CH), 227.9 (C=S). EI-MS: 190 (M^+, 15), 133 (74), 114 (58), 92 (46), 57 (100). Anal. Calcd for $C_7H_{10}O_2S_2$ (190.27): C, 44.19; H, 5.30; found: C, 44.15; H, 5.36%.

5-(Isopropoxymethyl)-1,3-oxazole-2-one (3g):

Pall yellow oil, yield: 0.37 g (96%). IR (KBr) (ν_{max}/cm^{-1}): 1703, 1643, 1452, 1417, 1372, and 1332 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.12 (6 H, *d*, ^3J = 6.1, 2 Me), 3.53-3.62 (2 H, *m*, CH_2), 3.73 (1 H, *m*, CH), 3.89 (1 H, *dd*, ^2J = 12.0, ^3J = 4.9, CH), 4.01 (1 H , *dd*, ^2J = 12.0, ^3J = 5.7, CH), 4.36-44.40 (1 H, *m*, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 21.7 (Me), 21.8 (Me), 44.7 (CH_2), 58.6 (CH_2), 67.0 (CH), 72.3 (CH), 227.3 (C=S). EI-MS: 192 (M^+, 5), 149 (84), 119 (25), 116 (52), 92 (32), 43 (42), 73 (100). Anal. Calcd for $C_7H_{12}O_2S_2$ (192.29): C, 43.72; H, 6.29; found: C, 43.85; H, 6.26%.

4,5-Diphenyl-1,3-oxazole-2-one (3h):

Yellow crystals, yield: 0.48 g (88%); mp 123-125°C. IR (KBr) (ν_{max}/cm^{-1}): 1475, 1435, 1140, and 1050 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 4.41 (1 H, *s*, CH), 5.74 (1 H, *s*, CH), 7.13-7.17 (5 H, *m*, 5 CH), 7.31-7.33 (5 H, *m*, 5 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 44.5 (CH), 70.6 (CH), 127.6 (CH), 128.1 (2 CH), 128.5 (2 CH), 129.5 (2 CH), 129.6 (CH), 129.8 (2 CH), 133.6 (C), 135.5 (C), 225.3 (C=S). EI-MS: 272 (M^+, 15), 196 (78), 180 (64), 92 (58), 77 (100). Anal. Calcd for $C_{15}H_{12}OS_2$ (272.38): C, 66.15; H, 4.44; found: C, 66.08; H, 4.39%.

4,5-Diphenyl-1,3-oxazole-2-one (3i):

Yellow crystals, yield: 0.47g(86%); mp 127-129°C. IR (KBr) (ν_{max}/cm^{-1}): 1479, 1439, 1142, and 1056 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 4.08 (1 H, *s*, CH), 5.76 (1 H, *s*, CH), 7.00 (2 H, *d*, ^3J = 7.4, 2 CH), 7.18 (2 H, *t*, ^3J = 7.8, 2 CH), 7.27-7.30 (3 H, *m*, 3 CH), 7.38 (2 H, *t*, ^3J = 7.5, 2 CH), 7.54 (1 H, *d*, ^3J = 7.4, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 45.9 (CH), 68.4 (CH), 126.9 (2 CH), 128.0 (CH), 128.8 (2 CH), 129.1 (2 CH), 129.2 (2 CH), 129.3 (CH), 133.5 (C), 137.7 (C), 227.9 (C=S). EI-MS: 272 (M^+, 15), 196 (76), 180 (62), 92 (62), 77 (100). Anal. Calcd for $C_{15}H_{12}OS_2$ (272.38): C, 66.15; H, 4.44; found: C, 66.08; H, 4.46%.

References

[1] Do¨mling, A. *Comb. Chem. High Throughput Screening* **1998**, *1*, 1.
[2] Do¨mling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3169.
[3] Weber, L. *Drug Discovery Today* **2002**, *7*, 143.
[4] Zhu, J., *Multicomponent Reactions;* Bienayme, H., Eds.; Wiley-VCH: Weinheim, Germany, **2005**.
[5] Wipf, P.; Kendall, C. *Chem. Eur. J.* **2002**, *8*, 1779.
[6] Balme, G.; Bossharth, E.; Monteiro, N. *Eur. J. Org. Chem.* **2003**, 4101.
[7] Jacobi von Wangelin, A.; Neumann, H.; Gordes, D.; Klaus, S.; Strubing, D.; Beller, M. *Chem. Eur. J.* **2003**, *9*, 4286.
[8] (a) Domling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168; (b) Ugi, I.; Domling, A. *Endeavour* **1994**, *18*, 115; (c) Heck, S.; Domling, A. *Synlett* **2000**, 424.
[9] Weber, L. *Curr. Med. Chem.* **2002**, *9*, 2085.
[10] Cave, G. W. V.; Raston, C. L.; Scott, J. L. *Chem. Commun*. **2001**, 2159.
[11] Sheldon, R. A. *Chem. Ind.* **1997**, 12.
[12] Eftekhari-Sis, B.; Zirak, M.; Akbari, A. *Chem. Rev.* **2013**, 113, 2958.
[13] Ansari, A.; Ali, A.; Asif, M. *New J. Chem.* **2017**, *41*, 16.
[14] JuYandVarma, R. S. *J. Org. Chem.* **2006**, *71*, 135
[15] Zárate-Zárate, D.; Aguilar, R.; Hernández-Benitez, R. I.; LabarriosEM,Delgado, F.; Tamariz, J. *Tetrahedron* **2015**, 71, 6961.
[16] Gordon, E.M.; Barrett, R.W.; Dower, W.J.; Fodor, S. P. A.; Gordon, M. A. Gallop *J. Med. Chem.* **1994**, *37*, 1385.
[17] Ardiansah, B. *Asian J. Pharm. Clin. Res.* **2017**, *12*, 45.
[18] Srivastava, M.; Singh, J.; Singh, S. B.; Tiwari, K.; Pathak, K. V.; Singh, J. *Green Chem.* **2012**, *14*, 901.
[19] Pai, G.; Chattopadhyay, A. P. *Tetrahedron Lett.* **2016**, *57*, 3140.
[20] Bekhit, A. A.; Hassan, A. M.; Abd El Razik, H. A.; El-Miligy, M. M.; El-Agroudy, E. J.; Bekhit, Ael-D. *Eur. J. Med. Chem.* **2015**, 94, 30.
[21] Sony, J. K.; Ganguly, S. *Int. J. Pham Pharm. Sci.* **2016**, *8*, 75.
[22] Surendra, Kumar R.; Arif, I. A.; Ahamed, A.; Idhayadhulla, A. *Saudi J. Biol. Sci.* **2016**, *23*, 614.
[23] Alam, R.; Wahi, D.; Singh, R.; Sinha, D.; Tandon, V.; Grover, A.; Rahisuddin *Bioorg. Chem.* **2016**, *69*, 77.
[24] Shamsuzzaman, S.; Siddiqui, T.; Alam, M. G.; Dar, A. M. *J. Saudi Chem. Soc.* **2015**, *19*, 387.
[25] Saisal, M.; Hussain, S.; Haider, A.; Saeed, A.; Larik, F. A. *Chem. Pap.* **2018**, *73*, 1053.
[26] Kees, K. L.; Fitzgerald, J. J.; Steiner, K. E.; Mihan, B.; Tosi, T.; Mondoro, D.; McCaleb, M. L. *J. Med. Chem.* **1996**, *39*, 3920.
[27] Bailey, D. M.; Hansen, P. E.; Hlavac, A. G.; Baizman, E. R.; Pearl, J.; Defelice, A. F.; Feigenson, M. E. *J. Med. Chem.* **1985**, *28*, 256.
[28] Michon, V.; Penhoat, C. H. D.; Tombret, F.; Gillardin, J. M.; Lepage, F.; Berthon, L.; *Eur. J. Med. Chem.* **1995**, *30*, 147.
[29] Wiley, R. H.; Wiley, P. *Pyrazolones, Pyrazolidones and Derivatives* (New York: Wiley) **1964**, p. 102
[30] Jamwal, A.; Javed, A.; Bhardwaj, V. *J. Pharm. BioSci.* **2013**, *3*, 114.
[31] Haufel, J.; Breitmaier, E. *Angew. Chem.* **1974**, *13*, 604.
[32] Heller, S. T.; Natarajan, S. R. *Org. Lett.* **2006**, *8*, 2675.