Asian Journal of Chemistry Vol. 22, No. 2 (2010), 1403-1406

Synthesis of Some Derivatives of 4,5-Dihydrooxazoles

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Benzaldehyds with sodium amide in the presence of thiourea in tetrahydro furan at room temperature gave various 2,4,5-triphenyl-4,5-dihydrooxazoles. The thiourea-catalyzed condensation of the benzaldehyde yielded 2-amino-1,2-diphenylethanone. Reduction of 2-amino-1,2-diphenylethanone was performed with hydride from Cannizzaro reaction to give 2-amino-1,2-diphenylethanols. The 4,5-dihydrooxazole ring formation of the 2-amino-1,2-diphenylethanol and benzamide gave the desired 4,5-dihydrooxazole.

Key Words: 4,5-Dihydrooxazoles, Benzaldehyds, Thiourea.

INTRODUCTION

The synthetic utility of oxazolines has been demonstrated by their successful application to the synthesis of β-amino-α-hydroxy, γ-amino-β-hydroxy acids and biologically active natural products such as preussin[1], sphingofungin F [2], myriocin[3], spectaline[4], 1-deoxygalactonojirimycin[5], 1-deoxygulonojirimycin[6] and L-733, 060[7]. Recently all of the sphingosine and dihydroxysphingosine (sphinganine) analogues are reported to be potent inhibitors of protein kinase C (PKC) as well as stimulators of DNA synthesis and cell proliferation[8]. The wide spectrum of the biological activity of these molecules justified the efforts towards the synthesis of them as well as of their stereoisomers and various analogues[9-12]. In this study, a new procedure for formation of 2,4,5-triphenyl-4,5-dihydrooxazole and its derivatives ring from benzaldehyds and base [$NaNH_2$] in the presence of thiourea is described. The most significant point of this method is that it is based on the 2-amino-1,2-diphenylethanone formation under thiourea catalyzed condensation then reduction in the presence of base and aldehyde in one pot.

EXPERIMENTAL

General procedure for the syntheses of compounds 5-8: To a stirred solution of aldehydes **13-16** (0.01 mmol) in THF (5 mL) at room temperature was added $NaNH_2$ (0.01 mmol) followed by thiourea (0.01 mmol). The reaction mixture was stirred at room temperature. The reaction was monitored by TLC and after the disappearance of starting compounds, the reaction mixture was poured into water and extracted with diethyl ether (3 × 30 mL). The organic layers were dried over

Na_2SO_4 and evaporated under reduced pressure. Column purification (20-30 % EtOAc in petroleum ether) furnished the products **5-8**.

5a: ^{1}H NMR δ_H (250 MHz; $CDCl_3$): 5.7 (1H, d, *J* = 10 Hz), 6.0 (1H, d, *J* = 10 Hz), 7.0 (6H, m), 7.5 (3H, m), 8.2 (2H, m). ^{13}C NMR δ_C (63 MHz; $CDCl_3$): 74.9, 85.7, 126.7, 127.4, 127.8, 127.9, 128.1, 128.2, 128.3, 129.0, 129.1, 132.2, 137.0, 138.1, 165.3, MS (20 eV): m/z 300 (M^+, 25 %), 193 (100 %), 165 (85 %), 105 (55 %), 89 (95 %).

5b: ^{1}H NMR δ_H (250 MHz; $CDCl_3$): 5.2 (1H, d, *J* = 7.7 Hz), 5.4 (1H, d, *J* = 7.7 Hz), 7.4 (14H, m), 7.7 (1H, m). ^{13}C NMR δ_C (63 MHz; $CDCl_3$): 79.0, 89.0, 125.7, 126.7, 127.5, 127.8, 128.4, 128.5, 128.6, 128.8, 128.9, 131.7, 140.4, 141.9, 164.0.

6a: ^{1}H NMR δ_H (250 MHz; $CDCl_3$): 2.1 (3H), 2.2 (3H), 2.4 (3H), 5.6 (1H, d, *J* = 10 Hz), 5.9 (1H, d, *J* = 10 Hz), 6.8 (8H, m), 7.3 (2H, m), 8.0 (2H, m). ^{13}C NMR δ_C (63 MHz; $CDCl_3$): 21.0, 21.6, 74.0, 85.3, 124.8, 126.4, 127.8, 128.3, 128.4, 128.5, 129.2, 133.7, 134.9, 136.3, 136.9, 142.0, 164.8.

6b: ^{1}H NMR δ_H (250 MHz; $CDCl_3$): 2.3 (6H), 2.4 (3H), 5.1 (1H, d, *J* = 7.2 Hz), 5.3 (1H, d, *J* = 7.2 Hz), 7.2 (10H, m), 8.0 (2H, m). ^{13}C NMR δ_C (63 MHz; $CDCl_3$) : 21.1, 21.2, 21.6, 78.6, 88.9, 124.8, 125.7, 126.6, 128.5, 129.1, 129.5, 137.3, 137.6, 138.1, 139.2, 142.0, 163.9.

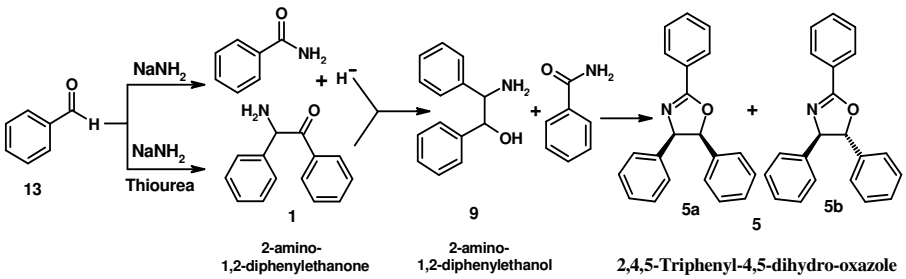
7: ^{1}H NMR δ_H (250 MHz; $CDCl_3$): 5.6 (1H, d, *J* = 10 Hz), 5.9 (1H, d, *J* = 10 Hz), 6.8 (8H, m), 7.3 (2H, m), 8.0 (2H, m). ^{13}C NMR δ_C (63 MHz; $CDCl_3$): 21.0, 21.6, 74.0, 85.3, 124.8, 126.4, 127.8, 128.3, 128.4, 128.5, 129.2, 133.7, 134.9, 136.3, 136.9, 142.0, 164.8.

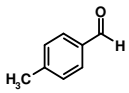
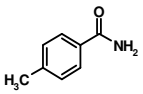
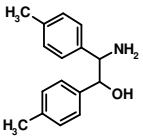
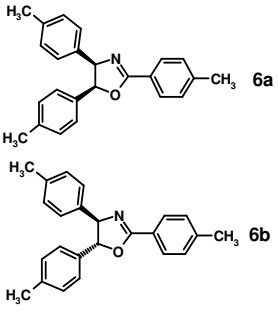
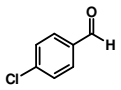
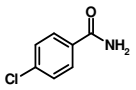
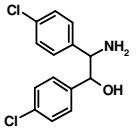
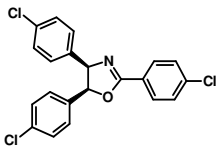
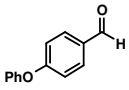
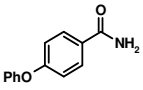
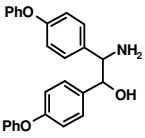
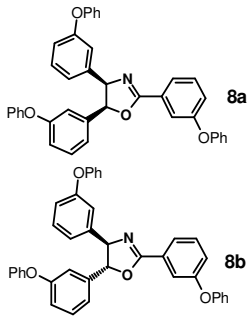
8a: ^{1}H NMR δ_H (250 MHz; $CDCl_3$): 5.7 (1H, d, *J* = 10 Hz), 5.9 (1H, d, *J* = 10 Hz), 6.6 (2H, m), 6.7 (7H, m), 7.1(6H, m) 7.2(7H, m) 7.8 (1H), 7.9 (2H). ^{13}C NMR δ_C (63 MHz; $CDCl_3$): 78.7, 88.5, 116.0, 117.4, 118.1, 118.4, 118.8, 118.9, 119.1, 119.5, 120.1, 121.5, 122.3, 123.4 123.5, 123.6, 128.8, 129.0, 129.7, 129.8, 129.9, 130.2, 130.4, 130.9, 130.9, 132.5 142.2, 143.7, 156.7, 156.9, 157.0, 157.4.

8b: ^{1}H NMR δ_H (250 MHz; $CDCl_3$): 5.1 (1H, d, *J* = 7.5 Hz), 5.3 (1H, d, *J* = 7.5 Hz), 7.1 (14H, m), 7.3 (8H, m), 7.7(1H). 7.8 (1H). ^{13}C NMR δ_C (63 MHz; $CDCl_3$) : 78.7, 88.5, 115.9, 117.4, 118.0, 118.4, 118.8, 118.9, 119.0, 120.1, 121.5, 122.3, 123.3, 123.5, 123.6, 129.0, 129.7, 129.8, 129.9, 130.2, 130.3, 142.2, 143.7, 156.7, 156.9, 157.0, 157.4, 157.6, 157.8, 163.7.

RESULTS AND DISCUSSION

The synthesis of of *trans* and *cis* 4,5-dihydrooxazole **5-8** is depicted in **Scheme-I**. The benzamides **9-12** were converted to the corresponding 4,5-dihydrooxazoles **5-8** by treating with amino alcohol **1-4**. One pot synthesis of amino alcohols **1-4** were prepared from the benzaldehydes **13-16** according to the known benzoin condensation procedure as shown in **Scheme-I**. Reduction of benzoins with hydride ion from Cannizaro reaction gave the corresponding amino alcohol, which was reacted with benzamide **9-12** in THF at room temperature to afford *trans* and *cis*-4,5-dihydro-oxazole. The thiourea-catalyzed condensation of the benzaldehyde yielded the



Aldehydes	Arylamides	2-Amino-1,2-diarylethanols	4,5-Dihydrooxazoles
 **14**	 **10**	 **2**	 **6** 2,4,5-Tri-*p*-tolyl-4,5-ihydrooxazole
 **15**	 **11**	 **3**	 **7** 2,4,5-Tris(4-chlorophenyl)-4,5-dihydrooxazole
 **16**	 **12**	 **4**	 8 2,4,5-*Tris*(3-phenoxyphenyl)-4,5-dihydrooxazole

Scheme-I

2-amino-1,2-diphenylethanone. Reduction of 2-amino-1,2-diphenylethanone was performed with hydride from Cannizzaro reaction to give threo and erythro 2-amino-1,2-diphenylethanol. The 4,5-dihydrooxazole ring formation of the 2-amino-1,2-diphenylethanol and benzamide gave the desired 4,5-dihydrooxazole as *cis* and *trans* diastereomer.

In the ^{1}H NMR spectrum of compounds **6-8** recorded in $CDCl_3$ solution at 25 ºC observed two separate sets of resonances attributable to each of the two hydrogens on the 4,5-dihydrooxazole ring. The twin resonance of the hydrogens on the *cis*-4,5-dihydrooxazole ring resonated in the range δ 5.8-6.0, with coupling constant 10 whereas in all of the other *trans*-4,5-dihydrooxazole, the resonances appeared in the range of δ 5.2-5.5, with coupling constant 7.

In summary, we report an efficient and short synthetic method for 2,4,5-triaryl-4,5-dihydrooxazoles from commercially available aldehydes. The key steps are the simple *in situ* preparation of 2-amino-1,2-diarylethanols and arylamides.

REFERENCES

1. K.Y. Lee, Y.H. Kim, C.Y. Oh and W.H. Ham, *Org. Lett*., **25**, 4041 (2000).
2. K.Y. Lee, C.Y. Oh and W.H. Ham, *F. Org. Lett*., **25**, 4403 (2002).
3. K.Y. Lee, C.Y. Oh, Y.H. Kim, J.E. Joo and W.H. Ham, *Tetrahedron Lett.*, **43**, 9361 (2002).
4. Y.S. Lee, Y.H. Shin, Y.H. Kim, K.Y. Lee, C.Y. Oh, S.J. Pyun, H.J. Park, J.H. Jeong and W.H. Ham, **14**, 87 (2003).
5. S.J. Pyun, K.Y. Lee, C.Y. Oh and W.H. Ham, *Heterocycles*, **62**, 333 (2004).
6. S.J. Pyun, K.Y. Lee, C.Y. Oh, J.E. Joo, S.H. Cheon and W.H. Ham, *Tetrahedron*, **61**, 1413 (2005).
7. Y.J. Yoon, J.E. Joo, K.Y. Lee, Y.H. Kim, C.Y. Oh and W.H. Ham, *Tetrahedron Lett*., **46**, 739 (2005).
8. Y.A. Hannun, Sphingolipid-Mediated Signal Transduction, Chapman-Hall, New York (1997).
9. A. Sharma, S. Gamre and S. Chattopadhyay, *Tetrahedron Lett.*, **48**, 633 (2007).
10. B. Olofsson and P. Somfai, *J. Org. Chem*., **68**, 2514 (2003).
11. G.R. Cook and K. Pararajasingham, *Tetrahedron Lett.*, **43**, 9027 (2002).
12. M. Masuia and T. Shioiri, *Tetrahedron Lett.*, **39**, 5199 (1998).

(*Received*: 4 May 2009; *Accepted*: 28 October 2009) AJC-7997