Chinese Chemical Letters Vol. 14, No. 2, pp 133 – 134, 2003 133
http://www.imm.ac.cn/journal/ccl.html

An Abnormal Reaction of N- (2,4-dinitrophenyl)-L-proline with Thionyl Chloride

Zhi Bin XU, Zong Ru GUO*

Institute of Materia Medica, Chinese Academy of Medical Sciences
& Peking Union Medical College, Beijing 100050

Abstract: N- (2,4-Dinitrophenyl)-4-amino-n-butyl aldehyde **3** was obtained with high yield of 80% when N- (2,4-dinitrophenyl)-L-proline **1** reacted with $SOCl_2$ at room temperature. However, the anticipated product N- (2,4-dinitrophenyl)-tetrahydropyrrolyl-2- (4-methylthiophenyl) ketone **2** did not be produced. The mechanism was discussed in this article.

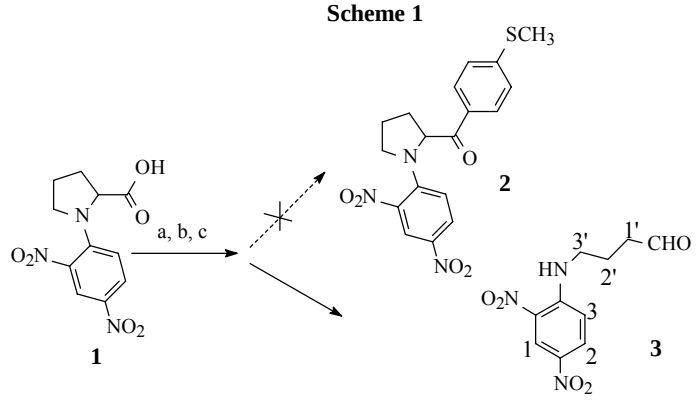
Keywords: L-Proline, 1-fluoro-2,4-dinitrobenzene(FDNB), N-(2,4-dinitrophenyl)-4-amino-*n*-butyl aldehyde.

Being a reactive aryl halide, 1-fluoro-2, 4-dinitrobenzene (FDNB) can react with functional groups such as imidazoles, α- or β- amino groups of peptides. So it has been widely used in structural and functional studies of peptide and protein[1]. Shaltiel [2] reported that dinitrophenyl moiety could be removed by the treatment of 2-mercaptoethanol under mild condition. We tried to use the FDNB as a protective group to prepare compound **2** by Friedel-Crafts acylation. However, aldehyde **3** in brown color was obtained with excellent yield of 80%, after the reaction mixture was treated with ice cooled dilute HCl. Its structure was confirmed unambiguously through ^{1}H-NMR, MS, and IR spectra[3] (**Scheme 1**).

Compound **1** was synthesized from L-proline according to the literature[4] with the yield of 90%. Compound **1** (0.56 g, 1.9 mmol) was stirred about 30 minutes with thionyl chloride (0.50 mL, 6.8 mmol) at room temperature and then quenched by the ice cooled dilute HCl. The mixture was extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. Removal of the solvents *in vacuo* and the residue was recrystallized from ether/CH_2Cl_2 (1:1) gave compound **3** (0.62 g, 81.2%,). The mechanism of the formation of aldehyde **3** is proposed as follows: as a tentative intermediate, acyl chloride **4** decomposed into carbon monoxide and the imminium ion **5** at room temperature with the aid of delocalization of the lone electron pair of nitrogen as driving force. Hydrolysis of **5** gave the unexpected N- (2,4-dinitrophenyl) -4-amino-n-butyl aldehyde **3** (**Scheme 2**). The role of the dinitrophenyl moiety in the reaction is to be explored.

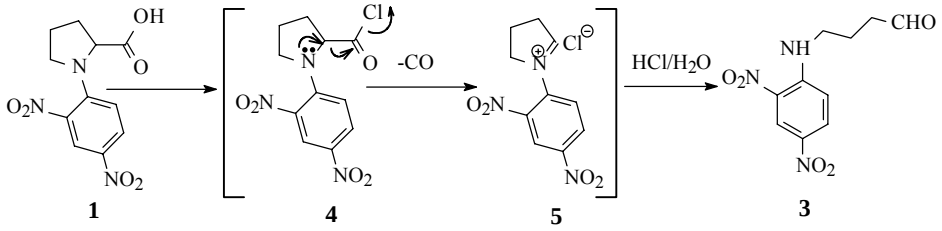
*E-mail: zrguo@imm.ac.cn

Scheme 1



a. $SOCl_2$, room temperature; b. $AlCl_3$, Thioanisole, room temperature; c. HCl, H_2O.

Scheme 2



References and Notes

1. M. Sokolovsky, T. Sadeh, A. Patchornik, *J. Am. Chem. Soc.*, **1964**, *86*, 1212.
2. S. Shaltiel, *Biochem. Biophys. Res. Commun.*, **1967**, *29*, 178.
3. Data of compound **3**: mp 94-95°C; ^{1}H-NMR (300M, $CDCl_3$, δ_{ppm}): 9.86 (s, 1H, CHO), 9.14 (d, 1H, J=2.4Hz, H-1), 8.61 (br, s, 1H, NH, exchanged by D_2O), 8.30 (dd, 1H, J=10.5, 2.4Hz, H-2), 7.02 (d, 1H, J=10.5Hz, H-3), 3.47 (m, 2H, H-3′), 2.70 (t, 2H, J=6.3Hz, H-1′), 2.09(m, 2H, H-2′); EI-MS (*m/z*): 253 (M^+), 225 (M^+-CO), 196 (100, M^+-CH_2CH_2CHO); IR (KBr, cm^{-1}): 3379 (NH), 2841,2740,1716 (CHO);
4. C. Paul, C. Bertrand, *GB patent* 1315633

Received 15 April, 2002