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Research Article

Effective Use of Oxalyl Chloride Compound in Synthesis of Oxalohydrazide and Parabanic Acid Derivatives

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Abstract

Oxalyl chloride, $(COCl)_2$, as an easily available chemical, is one of the organic reagents that are highly applicable in chemical reactions. It is used as the starting material of various chemical transformations such as ring closure in organic reactions, ring opening of epoxides, chlorination, and formylation. In this context, we report the reactions of oxalyl chloride (1) with cyanoacetyl hydrazide (2) and N,N'-diarylcarbazone (3) for the first time here. Compounds (4 and 5) characterized by elemental analysis, ^{1}H, and ^{13}C-NMR spectra are conformable by structure.

Keywords: Oxalyl chloride, Carbazone, Cyanoacetyl hydrazide, Oxalohydrazid, Parabanic acid

1. INTRODUCTION

Oxalyl chloride, whose IUPAC name is ethanedioyl dichloride, is a unique reagent in the synthesis reactions of organic chemistry. This reagent is also called oxalic acid chloride or oxalyl dichloride. This liquid, melting at 16°C and boiling at 63–64°C, is a colourless compound with a pungent odor. It dissolves very well in organic solvents such as dichloromethane, acetonitrile, chloroform, diethyl ether, benzene, and hexane. This compound is highly sensitive to moisture as it reacts violently with water [1].

The French chemist Adrien Fauconnier obtained oxalyl chloride for the first time in 1992 as a result of the reaction of phosphorus pentachloride (PCl_5) with diethyl oxalate [2]. Although oxalyl chloride appears to be a small and simple molecule, it is a widely used reagent in organic chemistry synthesis because actually the two chlorine atoms in its structure can be easily separated [2]. Oxalyl chloride has great importance, especially in the synthesis of five-ring, six-ring, seven-ring, and octa-ring structures that form 1,2-dicarbonyl compounds consequently separation of two chlorine atoms. 1,2-dicarbonyl compounds exist in the chemical structure of natural products. such as Licoagrodione, Tanshinone IIA, Mansonone C, and Sophorradione, and drug molecules such as Indibulin, Biricodar, Boceprevir, and Fluocortin butyl (Figure 1) [3–10].

In this context, we report the reactions of oxalyl chloride (1) with cyanoacetyl hydrazide (2) and N,N'-diarylcarbazone (3) for the first time here Scheme 1. Compounds characterized using elemental analysis, ^{1}H-NMR and ^{13}C-NMR spectroscopy are consistent with the structure.

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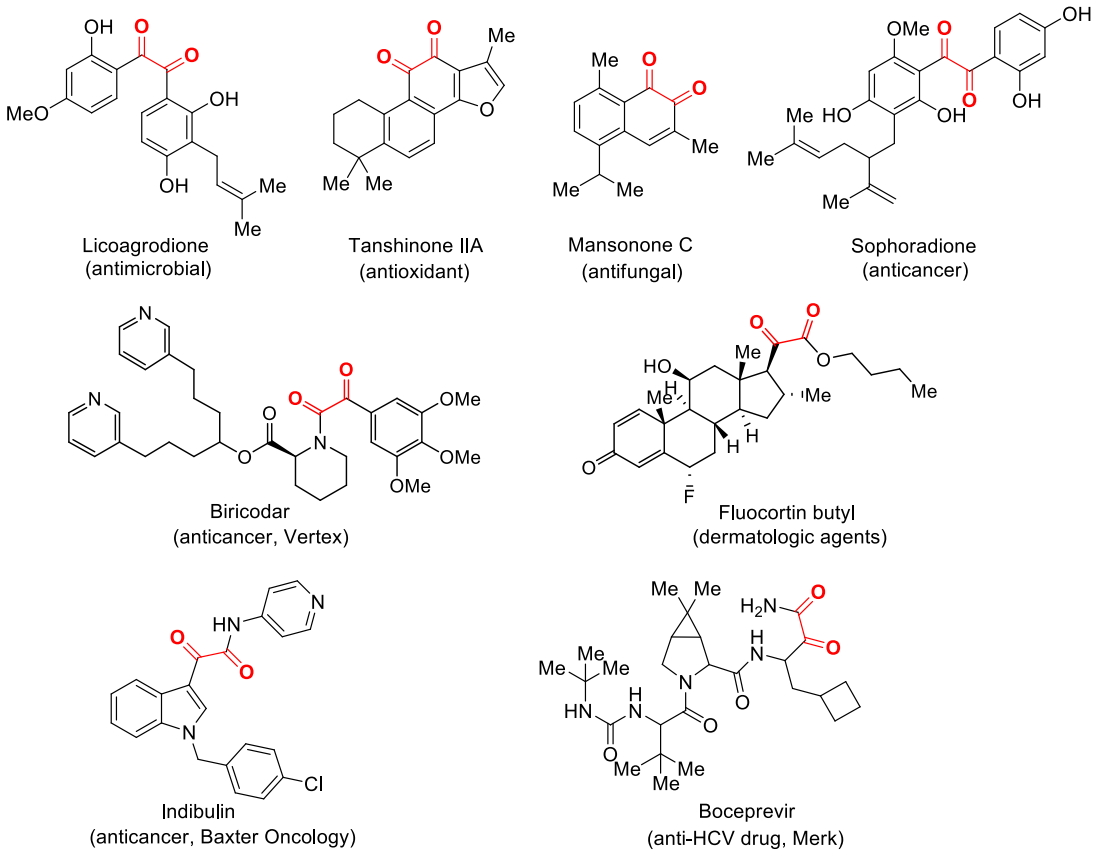
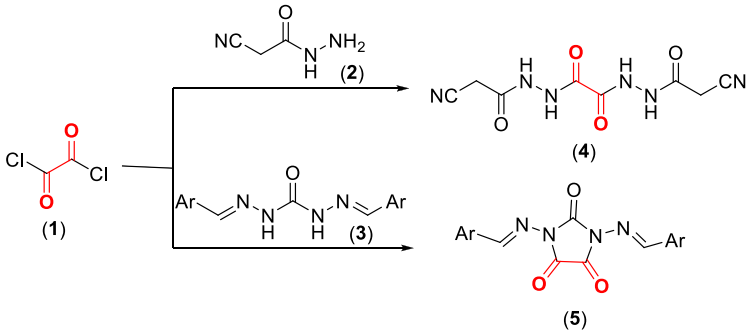


Figure 1. 1,2-Dicarbonyl-containing natural products and drug molecules



Scheme 1. Synthesis of compounds 4 and 5.

2. MATERIAL AND METHODS

The main chemicals used in our experiments are special reagents imported from companies such as Merck, Aldrich, Fluka and Sigma, and they are of analytical purity. Benzene, toluene, ethanol, etc. obtained from domestic producers in the reaction medium and purification processes. On the other hand, organic solvents were purified and used in our laboratory as a result of various processes. Unconfirmed melting points were recorded using an Electrothermal 9200 digital melting point instrument. Microanalyses were carried out using Leco-932 CHNS-O Elementel analyser. The ^{1}H- and ^{13}C-NMR analyses were performed with the help of Bruker Avance III 400MHz spectrometer using $CDCl_3$ or DMSO solvents.

2.1 General Procedure for the Synthesis of Products 4 and 5

1.00 mmol of nucleophiles (2, 3) with about 30 mL of acetonitrile was dissolved under reflux. Dissolved in 5 mL of acetonitrile on the 0.085 mL oxalyl chloride (1) was added drop wise. After the reaction was refluxed for 3 hours, the reaction solvent was removed using a rotary evaporator. The resulting oily product by adding absolute ether was stirred overnight at room conditions and filtered. The crude product obtained was crystallized from H_2O.

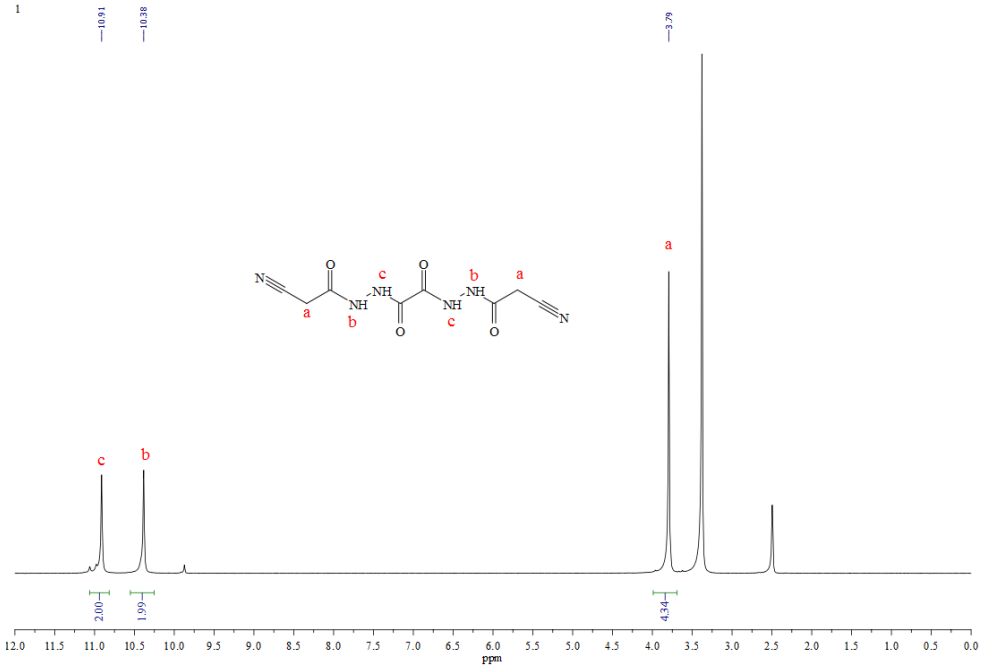


Figure 2. ^{1}H-NMR spectrum of compound (4)

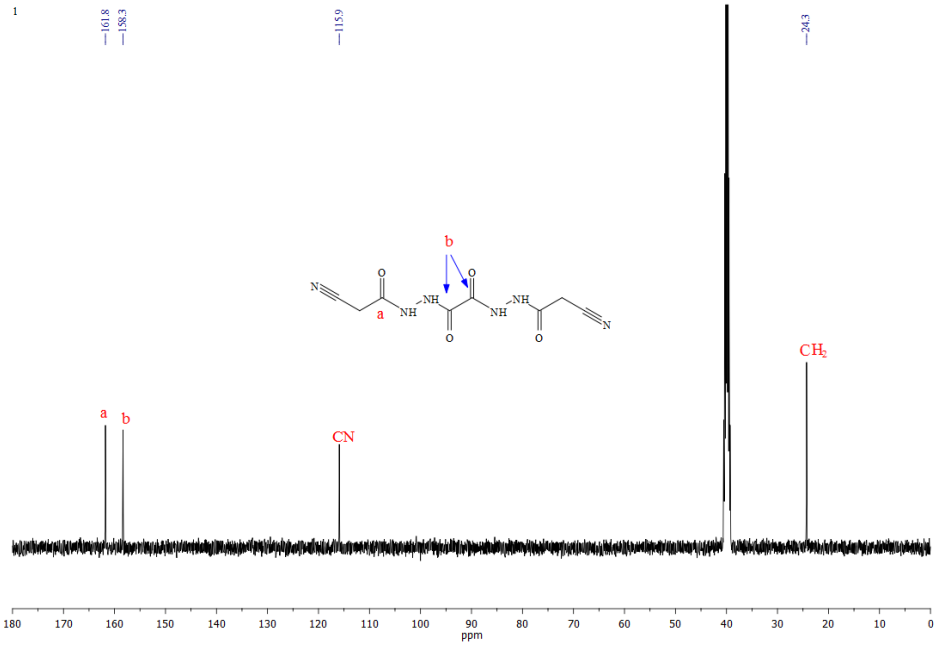


Figure 3. ^{13}C-NMR spectrum of compound (4)

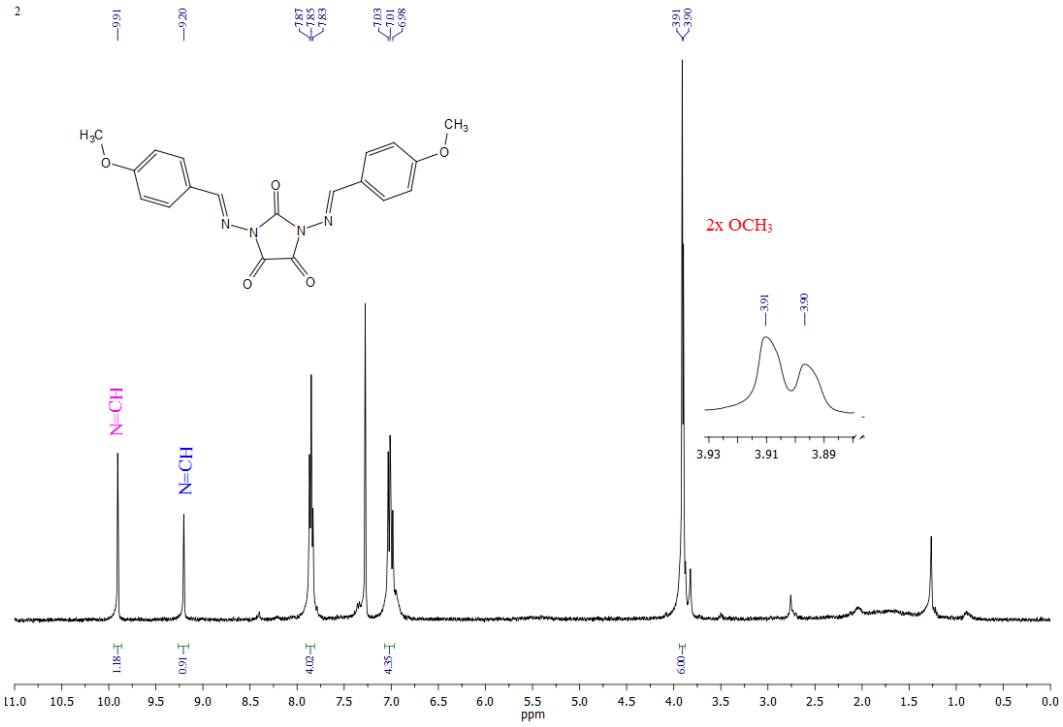


Figure 4. ^{1}H-NMR spectrum of compound (5)

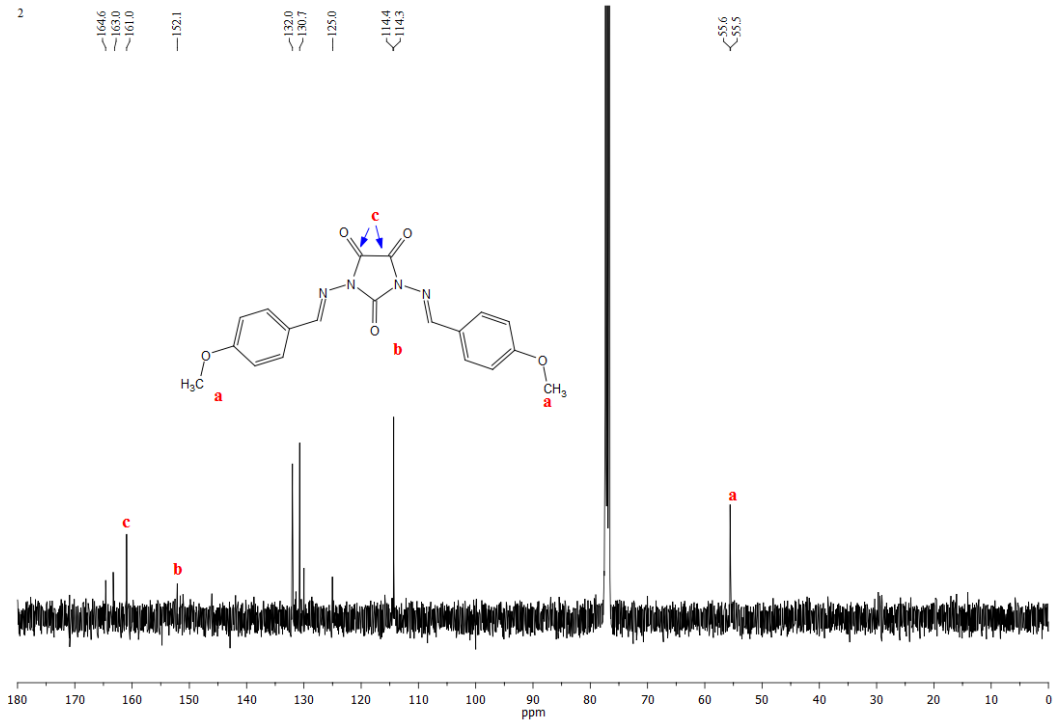


Figure 5. ^{13}C-NMR spectrum of compound (5)

2.2 N'1,N'2-bis(2-cyanoacetyl)oxalohydrazide (4)

White crystals, 168 mg, 67% yield; mp 151–153 °C. ^{1}H-NMR (DMSO–d_6) δ ppm: 10.92, 10.39 (s, 4H, NH), 3.80 (s, 2H, CH_2). ppm; ^{13}C-NMR (DMSO–d_6): 161.78 (-CH_2-CO-NH-), 158.32 (-NH-CO-CO-NH-), 115.92 (CN), 24,29 (-CH_2-). Anal. Calcd for $C_8H_8N_6O_4$ (252.19 g/mol): C, 38.10; H, 3.20; N, 33.32. Found: C, 38.32; H, 3.10; N, 33.19%.

2.3 1,3-bis((Z)-4-methoxybenzylideneamino)imidazolidine-2,4,5-trione (5)

White crystals, 332 mg, 75% yield; mp 173–175 °C. ^{1}H-NMR ($CDCl_3$–d_6) δ ppm: 9.90, 9.21 (s, CH=N), 7.87-6.98 (d, Ar-H), 3,90 (s, O-CH_3). ppm; ^{13}C-NMR ($CDCl_3$–d_6): 164.62 (C-O-CH_3), 163.29 (N-CO-CO-N), 160.95 (N-CO-N), 153.0 (N=CH), 132.00-114,32 (Ar-C), 55,51 (-OCH_3). Anal. Calcd for $C_{19}H_{16}N_4O_5$ (380.35 g/mol): C, 60.00; H, 4.24; N, 14.73. Found: C, 59.84; H, 4.14; N, 14.46%.

3. RESULTS AND DISCUSSION

Different synthesis methods have been developed for the synthesis of many organic compounds. 1,2-diketones have always attracted great interest in organic synthesis as intermediates with very useful functional groups that undergo a wide variety of chemical transformations. However, these oxalyl derivative compounds were used as the source of the α-dicarbonyl moiety. In Scheme 1, compounds (4) and (5) were obtained in good yield by reacting compound (1) with hydrazide (2) and carbazone compound (3). In the reaction, firstly, compounds (2) and (3) were reacted with oxalyl chloride (1) by boiling in acetonitrile under reflux for 3 hours. And then, the solvent was removed from the rotary evaporator, ether was added to the oily product, and stirred at room condition for one night. The crude solid product obtained at the end of this time was filtered and crystallized from pure water. The obtained compounds were characterized by spectroscopic methods. Each compound has three different carbonyl groups, and each has a different chemical environment. Looking at the ^{1}H-NMR spectrum of compound (4), proton signals belonging to NH and CH_2 groups emerged. When the ^{13}C-NMR spectrum was examined, the signals of acetyl carbonyl at δ 161.78 ppm, oxalyl carbonyls at 158.32 ppm, nitrile carbonyls at 115.92 ppm, and methylene carbonyls at 24.29 ppm were observed. Looking at the ^{1}H-NMR spectrum of compound (5), proton signals belonging to the aromatic ring, benzal, and methoxy groups observed. When the ^{13}C-NMR spectrum is examined, oxalyl carbonyls at δ 163.29 ppm, urea carbonyls at 160.95 ppm, benzal carbonyls at 153.0 ppm, aromatic ring carbonyls at 164.62, 132.00-114.32 ppm, and 55.51 ppm signals of methoxy carbonyls appeared in.

4. CONCLUSION

Looking at the studies conducted in recent years, it has been reported that 1,2-dicarbonyl molecules are in the structures of natural compounds and drug-active substances. In this study, oxalohydrazide and parabanic acid compounds were synthesized by the reaction of cyanoacetyl hydrazide and carbohydrazone compounds with oxalyl chloride. The obtained compounds were characterized by spectroscopic methods.

AUTHOR'S CONTRIBUTIONS

All authors have made essential contributions to this study. IEK: Writing, review and editing. The final version of the article has been read and approved by all authors.

CONFLICTS OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

RESEARCH AND PUBLICATION ETHICS

The author declares that this study complies with Research and Publication Ethics.

REFERENCES

[1] R. Salmon and I. V. Efremov, "in Encyclopedia of Reagents for Organic Synthesis," John Wiley & Sons, Weinheim, 2001.

[2] A. Fauconnier, "The Action of Phosphorus Pentachloride on Diethyl Oxalate," Comptes Rendus Acad. Sci., vol. 114, pp. 122–123, 1892.

[3] W. Li, Y. Asada, and T. Yoshikawa, "Antimicrobial Flavonoids from Glycyrrhiza Glabra Hairy Root Cultures," Planta Med., vol. 64, pp. 746–747, Dec. 1998, doi:10.1055/s-2006-957571.

[4] S. Jang, S. Jeung, K. Kim, H. Kim, H. Yu, R. Park, H. Kim, and Y. You, "Tanshinone IIA from *Salvia miltiorrhiza* Inhibits Inducible Nitric Oxide Synthase Expression and Production of TNF-α, IL-1β and IL-6 in Activated RAW 264.7 Cells," Planta Med., vol. 69, pp. 1057–1059, Nov. 2003, doi:10.1055/s-2003-45157.

[5] G. B. M. Bettòlo, C. G. Casinovi, and C. Galeffi, "A New Class of Quinones: Sesquiterpenoid Quinones of *Mansonia altissima Chev*," Tetrahedron Lett., vol. 52, pp. 4857–4864, 1965, doi: 10.1016/S0040-4039(01)89048-1.

[6] C. C. Shen, "Phenolic Constituents of the Roots of *Sophora flavescens*," J. Nat. Prod., vol. 69, pp. 1237–1240, Aug. 2006, doi:10.1021/np060189d.

[7] M. Knaack, P. Emig, J. W. Bats, M. Kiesel, A. Müller, and E. Günther, "Synthesis and Characterization of the Biologically Active 2-[1-(4-chlorobenzyl)-1H-indol-3-yl] -2-oxo-N-pyridin-4-yl acetamide," Eur. J. Org. Chem., vol. 2001, pp. 3843–3847, Sep. 2001, doi:10.1002/1099-0690(200110)2001:20<3843::AID-EJOC3843>3.0.CO;2-P.

[8] M. D. Armistead, W. M. Harding, J. O. Saunders, and S. J. Boger, "Biologically Active Acylated Amino Acid Derivatives," United States Patent. US 5723459, 1998.

[9] B. R. Bacon, S. C. Gordon, E. Lawitz, P. Marcellin, J. M. Vierling, S. Zeuzem. F. Poordad, Z. D. Goodman, H. L. Sings, N. Boparai, M. Burroughs, C. A. Brass, J. K. Albrecht, and R. Esteban, "Boceprevir for Previously Treated Chronic HCV Genotype 1 Infection," N. Engl. J. Med., vol. 364, pp. 1207–1217, Mar. 2011, doi:10.1056/NEJMoa1009482.

[10] T. F. Hartley, P. L. Lieberman, E. O. Meltzer, J. N. Noyes, D. S. Pearlman, and D. G. Tinkelman, "Efficacy and Tolerance of Fluocortin Butyl Administered Twice Daily in Adult Patients with Perennial Rhinitis," J. Allergy Clin. Immunol., vol. 75, pp. 501–507, Apr. 1985, doi:10.1016/s0091-6749(85)80024-5.