molbank

MDPI

Editorial

Editorial: Special Issue "Molecules from Side Reactions"

Stefano D'Errico

Department of Pharmacy, University of Naples Federico II, via D. Montesano, 49, 80131 Naples, Italy; stefano.derrico@unina.it

Received: 24 November 2020; Accepted: 27 November 2020; Published: 30 November 2020

Organic synthesis is a powerful tool that allows researchers to express their scientific creativity. Its fundamental role in obtaining drugs and creating new materials is irrefutable evidence. However, a chemical process may often take a side route, generating novel unexplored products. Most chemical reactions produce side products, which are often set aside and even thrown away. If the side product is formed in large amounts or if its presence makes difficult the chromatographic purification procedures, the desire to throw it away is even stronger. Let us suppose that a chemist is in the middle of a total synthesis made up of several synthetic steps and that, during a key step, he or she notes on thin layer chromatography (TLC)the formation of an intense spot with Rf that, in their knowledge, cannot belong to the target compound. At first glance, this side product, generated by a side reaction, could be discouraging and frustrating; however, the isolation and characterization of that product could give the possibility to better investigate the mechanism of reaction. The obtainment of a side product cannot fail to fascinate a chemist that works in the field of synthesis as (i) novel reactions may be discovered and (ii) novel molecular scaffolds may be achieved. The purpose of the Special Issue "Molecules from Side Reactions" was to collect papers reporting on the synthesis and characterization of those products that could be useful building blocks for the whole scientific community. The Special Issue was launched in July 2019 and collected 13 contributions by the end of 2020. The authors contributing to this Special Issue, whom the Guest Editor sincerely thanks, described the science elegantly and rationally; in addition, they characterized the side products according to the rigorous standards of Molbank. The published papers cover the following aspects of the organic chemistry field:

- Synthesis of Heterocycles
- Synthesis of Carbohydrates
- Synthesis of Modified Nucleosides
- C-H Bond Functionalization
- Mechanisms of Reactions

In the first paper, an oxidative ring opening reaction was reported to convert a disubstituted furan ring to isoxazole [1]. This reaction could be useful for the construction of linked isoxazoles and other new complex structures containing an isoxazole subunit. In the second paper, the nitration of pyridine-imidazolium salt was described. It proceeded with the oxidative cleavage of a N–C bond between imidazolium ring and methylene group, with the formation of two side products [2]. In the third paper, the authors described the access to the rare D- and L-psicose derivatives via hydroxy methylation of the ribono lactone [3]. The fourth paper dealt with the synthesis of an intriguing side product obtained during the 5′-ribose fluorination of the nucleoside 6-chloropurine riboside [4]. This reaction occurred during the preparation of a valuable, more lipophilic, analogue of the imidazo-nucleoside AICAR [5]. In the fifth paper, the synthesis of a *N*-(2-hydroxy-1,1-dimethylethyl)-3-methylbenzamide was accomplished. The importance of the compound lies in its potential reactivity as an

N,*O*-bidentate directing group in metal-catalyzed C–H bond functionalization reactions [6]. In the sixth paper, an interesting and unexpected obtainment of *N*′-acetylhydrazides from hydrolysis of the 3-acetyl-2,3-dihydro-1,3,4-oxadiazole derivatives of 1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine nucleus was presented [7]. In the seventh paper, an unexpected epoxide-oxetane rearrangement was observed during the synthesis of symmetrical dodeco-6,7-diuloses, that are potential candidates for inhibition of glycosidases [8]. In the eighth paper, a novel glycosyl sulfoxide was synthesized from a *S*-phenyl thioglycoside for the preparation of alginate oligosaccharides [9]. In the ninth paper, the authors discovered that the incorporation of 8-fluoro-*N*-2-isobutyryl-2′-deoxyguanosine into oligonucleotides through the phosphoramidite chemistry-based solid phase synthesis failed to give the desired products. These results prompted the authors to explore an alternative *N*-protecting group and to modify the solid phase synthetic cycle conditions [10]. In the tenth paper, the authors focused on the synthesis of peptidyl nucleosides as antibacterial agents. During their study to prepare an intermediate to be attached to a solid support, they found an interesting side product with a seven-membered ring [11]. In the eleventh paper, the formation of an isomeric mixture of dienynes, instead of a diallene, was detected during a reduction reaction performed on the 1,1,2,2,7,7,8,8-octaethoxyocta-3,5-diyne [12]. In the twelfth paper, the authors reported on the synthesis of a new pyrrole-substituted terpyridine derivative that possessed an allene moiety. It was obtained as an unexpected sole product during attempts to alkylate the *N*-atom of pyrrole [13]. In the last paper, the serendipitous formation of the cyclic guanidinium complex poly[1,3-dimethyltetrahydropyrimidin-2(1*H*)-iminium [tri-μ_2-cyanido-κ^6C:N-dicuprate(I)]] was found during an X-ray analysis of the crystals obtained after an attempted synthesis of a copper cyanide polymer involving the diamine *N*,*N*′-1,3-dimethyldiaminopropane [14]. All this research confirms the importance of isolating, characterizing and always preserving all the products formed during a reaction. A side product obtained from a side reaction could be as useful an intermediate as a novel pharmaceutical lead. Finally, special thanks go also to all the reviewers, who always helped the Guest Editor to make clear and final decisions, maintaining the high-quality standards of Molbank.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Sawengngen, N.; Kolodina, A.A.; Serdyuk, O.V. (*E*)-4-(3-Phenylisoxazol-5-yl)but-3-en-2-one. *Molbank* **2019**, *2019*, M1081. [CrossRef]
2. Cucu Diaconu, D.; Mangalagiu, V. Pyridine-imidazlolium salts: Oxidatively cleavage of N-C bond via nitration. *Molbank* **2019**, *2019*, M1095. [CrossRef]
3. Imrich, M.R.; Ziegler, T. Access to D-and L-psicose derivatives via hydroxy methylation of Ribono Lactone. *Molbank* **2019**, *2019*, M1096. [CrossRef]
4. Falanga, A.P.; Marzano, M.; Terracciano, M.; D'Errico, S. 5′-Chloro-5′-deoxy-2′,3′-*O*-isopropylidene-6-fluoro nebularine. *Molbank* **2019**, *2019*, M1097. [CrossRef]
5. D'Errico, S.; Oliviero, G.; Borbone, N.; Amato, J.; Piccialli, V.; Varra, M.; Mayol, L.; Piccialli, G. Solid-phase synthesis of a new diphosphate 5-aminoimidazole-4-carboxamide riboside (AICAR) derivative and studies toward cyclic AICAR diphosphate ribose. *Molecules* **2011**, *16*, 8110–8118. [CrossRef] [PubMed]
6. Al Mamari, H.H.; Al Lawati, Y. *N*-(2-Hydroxy-1,1-dimethylethyl)-3-methylbenzamide. *Molbank* **2020**, *2020*, M1099. [CrossRef]
7. Soares, J.C.A.V.; Dias, L.R.S. *N*′-Acetyl-3-methyl-1,6-diphenyl-1H-pyrazolo[3,4-b]pyridine-4-carbohydrazide. *Molbank* **2020**, *2020*, M1104. [CrossRef]
8. Bayer, M.; Maichle-Mössmer, C.; Ziegler, T. Unexpected formation of oxetanes during the synthesis of dodeco-6,7-diuloses. *Molbank* **2020**, *2020*, M1108. [CrossRef]
9. Dimitriou, E.; Miller, G.J. Synthesis and isolation of diastereomeric anomeric sulfoxides from a D-mannuronate thioglycoside building block. *Molbank* **2020**, *2020*, M1111. [CrossRef]
10. Solodinin, A.; Helmkay, J.; Ollivier, S.; Yan, H. 8-Fluoro-*N*-2-isobutyryl-2′-deoxyguanosine: Synthesis and Reactivity. *Molbank* **2020**, *2020*, M1119. [CrossRef]

11. Leyerer, K.; Koppermann, S.; Ducho, C. Unexpected seven-membered ring formation for muraymycin-type nucleoside-peptide antibiotics. *Molbank* **2020**, *2020*, M1122. [CrossRef]
12. Petrova, S.M.; Sydnes, L.K. Formation of an isomeric mixture of dienynes instead of a diallene. *Molbank* **2020**, *2020*, M1133. [CrossRef]
13. Husson, J.; Guyard, L. 4′-(*N*-(Propan-1,2-dienyl)pyrrol-2-yl)-2,2′:6′,2″-terpyridine. *Molbank* **2020**, *2020*, M1142. [CrossRef]
14. Corfield, W.R.; Dayrit, J.R. Poly[1,3-Dimethyltetrahydropyrimidin-2(1*H*)-iminium [tri-μ_2-cyanido-κ^6C:N-dicuprate(I)]]. *Molbank* **2020**, *2020*, M1170. [CrossRef]