

Proceeding Paper

# Plant-Derived Triterpenoid Functionalization: Synthesis of $\alpha$ -Acyloxycarboxamides <sup>†</sup>

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**Abstract:** The application of isocyanide-based multicomponent reactions (IMCRs) for triterpenoid functionalization has been little reported. Triterpenoids and their derivatives are an important class of natural products of interest in medicinal chemistry due to their potential applications as antibacterial, antifungal, and cytotoxic agents. Herein, we describe the use of ethanol as a solvent in the Passerini reaction for the functionalization of masticadienonic acid isolated from fruits and peduncles of *P. mexicana*. A small series of  $\alpha$ -acyloxycarboxamides was synthesized with moderate to good overall yields of 33 to 57%, evaluating and extending the scope of the aldehyde component.

**Keywords:** triterpenoid; IMCR; Passerini-3CR;  $\alpha$ -acyloxycarboxamide

## 1. Introduction

Triterpenoids are a large class of plant-derived natural products, with an inherent structural diversity [1]. They are widely distributed in the plant kingdom, especially in higher plants [2]. Approximately 55,000 compounds belonging to this group have been identified; however, very few have been investigated for therapeutic applications [3]. The prevention and treatment of cancer is the most studied property of triterpenoids. Other important aspects include their antimicrobial, antiviral, antifungal, antiparasitic, anti-inflammatory, etc., properties [4–9].

Multicomponent reactions (MCRs) are synthetic procedures where three or more substances react to form a product which contains all or most of the atoms from the starting materials [10]. In these procedures, a complex molecule is assembled in a one pot chemical step, providing a huge chemical diversity [11].

Among the diverse class of MCRs, those involving isocyanide reagents were some of the first to be discovered. Mario Passerini reported in 1921 the first isocyanide-based multicomponent reaction (IMCR), employing aryl isocyanides, ketones, and carboxylic acids to obtain  $\alpha$ -acyloxycarboxamides [12]. Almost 40 years later, Ivar Ugi presented his four-component reactions, in which an isocyanide, a carbonyl compound, an amine, and an isocyanide react to yield *bis*-amides [13].

In the field of combinatorial chemistry, the IMCRs are an important and versatile tool which have several advantages, such as atom economy, convergent design, ease of performance, and the generation of molecular diversity [14]. On the other hand, IMCR products can be versatile synthetic platforms for further structural diversification [15].

In recent years, IMCRs have been applied to the rapid and efficient functionalization of natural products, especially steroids, peptides, and glycosides [16]. However, there are only a few reports on the use of triterpenoids as components in IMCRs. Regarding the Passerini reaction, there are two reports where triterpenoids were either naturally functionalized



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or their derivatives were used as components (Figure 1) [17,18]. Triterpenoids and their amide derivatives have been extensively studied over the last few decades as an alternative for cancer treatment, due to their important cytotoxic properties [19].

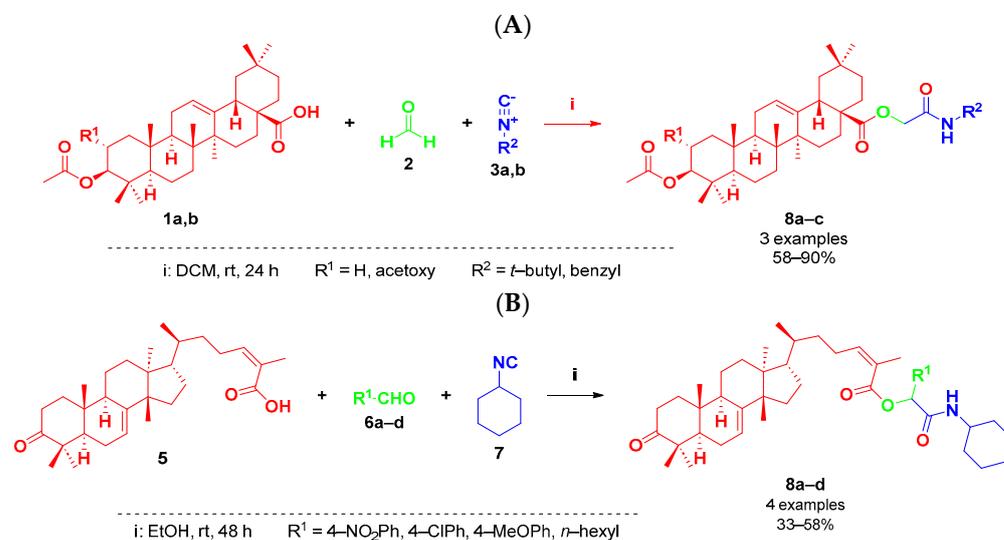


Figure 1. (A) Previous work by Wiemann, J., et al. (2018) [18]. (B) This work.

## 2. Results and Discussion

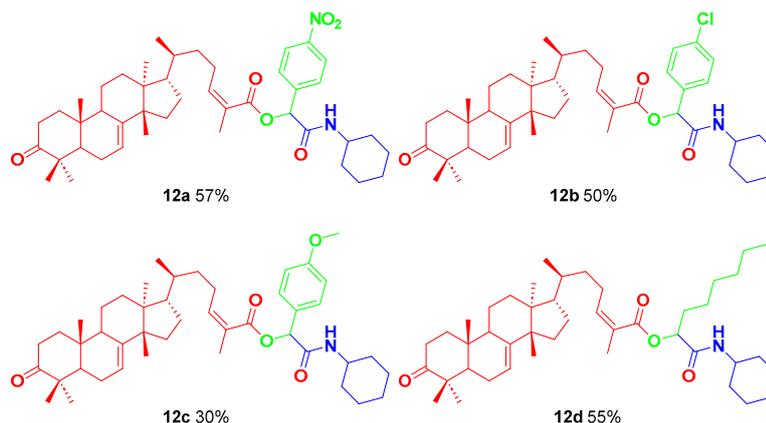
In the present work, we report the synthesis of a series of  $\alpha$ -acyloxycarboxamides employing a plant-derived triterpenoid as component in the Passerini three-component reactions. Masticadienonic acid (5) isolated from hexane extracts of fruits and peduncles of dried *P. mexicana*, along with 4-nitrobenzaldehyde (6a) and cyclohexyl isocyanide (7), was used as a component for reaction optimization to synthesize target molecule 8a. The performed experiments are depicted in Table 1.

Table 1. Screening conditions for the synthesis of target molecule 16a.

Entry	Solvent	Time	Yield
1	MeOH	48 h	30%
2	EtOH	48 h	57%
3	H <sub>2</sub> O	72 h	NR

In previous reports from our research group, dichloromethane was used as a solvent for the Passerini reaction; however, to improve the greenness of our procedures, we also utilized alternative solvents. There are some reports of the use of polar protic solvents for this methodology, for example methanol; however, this experiment led to a longer reaction time and a low yield of 30%. The starting material was not fully consumed, which might be a consequence of the poor solubility of compound 5. Another experiment using ethanol resulted in better yields (57%) since 5 is fairly soluble in this solvent. Finally, an experiment using water did not yield the desired product under the evaluated conditions.

Using the best conditions found in these experiments, a small library of  $\alpha$ -acyloxycarboxamides was synthesized, employing aromatic aldehydes with electron-donor and electron-withdrawing groups, as well as an aliphatic aldehyde.



### 3. Experimental Section

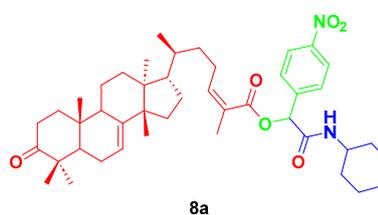
#### 3.1. General Information, Chemicals, and Instrumentation

Bruker Avance III spectrometers (500 and 125 MHz, respectively) were used for  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra acquisition. Deuterated chloroform ( $\text{CDCl}_3$ ) was used as the solvent for NMR experiments. Chemical shifts ( $\delta$ ) are given in ppm relative to tetramethylsilane (TMS). Coupling constants are reported in Hertz (Hz). The multiplicities of the signals are described using standard abbreviations: singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). NMR spectra were analyzed using MestReNova software version 12.0.0-20080. Reaction progress was monitored via thin-layer chromatography (TLC) on pre-coated silica gel F254 aluminum sheets. The spots were visualized under UV light at 254 nm. Column chromatography was performed using silica gel (230–400 mesh) as stationary phase. Mixtures of hexanes and ethyl acetate were used as mobile phase for column chromatography and in TLC for reaction progress monitoring and measuring retention factors ( $R_f$ ). All reagents were purchased from Sigma-Aldrich and were used without further purification. Chemical names and drawings were obtained using the ChemDraw 22.2.0.3300 software package.

#### 3.2. General Procedure

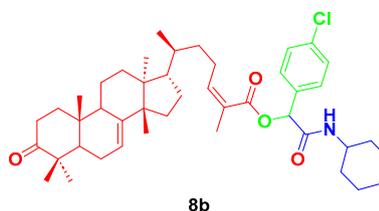
Masticadienonic acid (**5**, 1.0 equiv.), aldehyde **6a–d** (1.0 equiv.), and cyclohexyl isocyanide (**7**, 1.0 equiv.) were dissolved in ethanol (0.5 M) and placed in a sealed vial with a magnetic stir bar. The mixture was stirred at room temperature for 48 h. Then, solvent was removed under reduced pressure, and the crude reaction mixture was purified via column chromatography, using silica gel as stationary phase and a mixtures of ethyl acetate in hexanes, to yield the corresponding  $\alpha$ -acyloxycarboxamides **8a–d**.

#### 3.3. Spectral Data

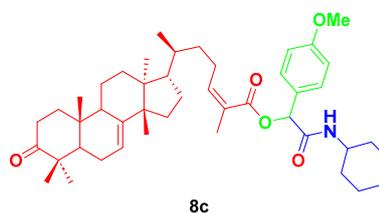


2-(cyclohexylamino)-1-(4-nitrophenyl)-2-oxoethyl-3-oxotirucalla-7,24Z-dien-26-oate (**8a**). White solid;  $R_f = 0.3$  (20% ethyl acetate in hexanes):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 25 °C, TMS):  $\delta$  8.23 (m, 2H), 7.63 (m, 2H), 6.14 (s, 1H), 6.10 (td,  $J = 7.6, 1.6$  Hz, 1H), 6.00 (s, 1H), 5.30 (dd,  $J = 6.1, 3.1$  Hz, 1H), 3.84 (dtt,  $J = 10.4, 7.8, 4.0$  Hz, 1H), 2.76 (td,  $J = 14.5, 5.5$  Hz, 1H), 2.59 (m, 1H), 2.45 (m, 1H), 2.28 (dt,  $J = 14.1, 3.8$  Hz, 1H), 2.25 (m, 1H), 2.10 (m, 2H), 2.07 (d,  $J = 1.5$  Hz, 3H), 1.99 (m, 2H), 1.98 (m, 1H), 1.98 (m, 4H), 1.81 (m, 2H), 1.73 (t,  $J = 8.7$  Hz, 1H), 1.69 (m, 2H), 1.64 (m, 1H), 1.56 (m, 2H), 1.53 (m, 2H), 1.49 (m, 1H), 1.48

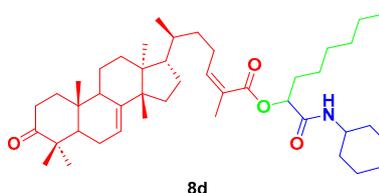
(m, 2H), 1.48 (m, 1H), 1.40 (m, 1H), 1.28 (m, 1H), 1.18 (m, 4H), 1.14 (m, 1H), 1.12 (s, 3H), 1.05 (s, 3H), 1.01 (s, 3H), 1.01 (s, 3H), 0.89 (d,  $J = 6.2$  Hz, 3H), 0.81 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  216.8, 166.3, 165.0, 148.9, 146.6, 145.88, 143.2, 127.9, 125.2, 123.7, 117.8, 74.2, 52.9, 52.3, 51.1, 48.4, 47.8, 47.7, 43.5, 38.5, 36.0, 35.6, 35.0, 34.9, 34.0, 33.63, 32.9, 28.2, 27.4, 26.9, 25.4, 24.6, 24.5, 24.3, 21.9, 21.6, 20.6, 18.2, 18.2, 12.7.



2-(cyclohexylamino)-1-(4-chlorophenyl)-2-oxoethyl-3-oxotirucalla-7,24Z-dien-26-oate (**8b**). Yellow oil;  $R_f = 0.31$  (20% ethyl acetate in hexanes):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 25 °C, TMS):  $\delta$  7.40 (m, 2H), 7.35 (m, 2H), 6.04 (d,  $J = 8.2$  Hz, 1H), 6.00 (dt,  $J = 7.6, 1.6$  Hz, 1H), 5.98 (d,  $J = 2.6$  Hz, 1H), 5.31 (dd,  $J = 6.0, 3.2$  Hz, 1H), 3.85 (dtt,  $J = 10.5, 7.8, 4.1$  Hz, 1H), 2.77 (td,  $J = 14.5, 5.4$  Hz, 1H), 2.58 (m, 1H), 2.45 (m, 1H), 2.29 (dt,  $J = 14.1, 3.7$ , 1H), 2.24 (m, 1H), 2.10 (m, 2H), 1.99 (m, 2H), 1.98 (m, 1H), 1.98 (d,  $J = 1.6$  Hz, 3H), 1.93 (m, 4H), 1.82 (m, 1H), 1.73 (t,  $J = 8.7$  Hz, 1H), 1.69 (m, 2H), 1.65 (m, 1H), 1.56 (m, 2H), 1.53 (m, 2H), 1.51 (m, 1H), 1.48 (m, 2H), 1.47 (m, 1H), 1.40 (m, 1H), 1.36 (s, 9H), 1.29 (m, 1H), 1.18 (m, 4H), 1.14 (m, 1H), 1.12 (s, 3H), 1.06 (s, 3H), 1.01 (s, 3H), 1.00 (s, 3H), 0.89 (d,  $J = 6.2$  Hz, 3H), 0.80 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  216.8, 167.3, 165.7, 146.6, 145.9, 135.0, 134.5, 129.1, 128.8, 125.2, 117.9, 73.9, 52.9, 52.3, 51.2, 48.5, 47.9, 47.7, 43.5, 38.5, 36.1, 35.7, 35.0, 34.9, 34.1, 33.6, 33.0, 28.3, 27.4, 27.0, 25.4, 24.7, 24.5, 24.4, 22.0, 21.6, 20.7, 18.2, 18.2, 12.8.



2-(cyclohexylamino)-1-(4-methoxyphenyl)-2-oxoethyl-3-oxotirucalla-7,24Z-dien-26-oate (**8c**). Yellow oil;  $R_f = 0.38$  (20% ethyl acetate in hexanes):  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 25 °C, TMS):  $\delta$  7.34 (m, 2H), 6.87 (m, 2H), 6.09 (dt,  $J = 7.5, 1.2$  Hz, 1H), 6.02 (bs, 1H), 5.98 (d,  $J = 2.9$  Hz, 1H), 5.31 (dd,  $J = 6.1, 3.4$  Hz, 1H), 3.86 (dtt,  $J = 10.5, 7.7, 4.0$  Hz, 1H), 3.80 (s, 3H), 2.74 (td,  $J = 14.5, 5.4$  Hz, 1H), 2.59 (m, 1H), 2.44 (m, 1H), 2.28 (dt,  $J = 14.1, 3.8$ , 1H), 2.25 (m, 1H), 2.11 (m, 2H), 1.98 (m, 1H), 1.99 (m, 1H), 1.97 (d,  $J = 1.5$  Hz, 3H), 1.93 (m, 4H), 1.81 (m, 1H), 1.73 (t,  $J = 8.7$  Hz, 1H), 1.69 (m, 2H), 1.65 (m, 1H), 1.56 (m, 2H), 1.55 (m, 2H), 1.49 (m, 1H), 1.48 (m, 2H), 1.48 (m, 1H), 1.41 (m, 1H), 1.36 (s, 9H), 1.28 (m, 1H), 1.18 (m, 4H), 1.15 (m, 1H), 1.12 (s, 3H), 1.05 (s, 3H), 1.01 (s, 3H), 0.99 (s, 3H), 0.89 (d,  $J = 6.2$  Hz, 3H), 0.81 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  216.8, 166.3, 165.7, 159.8, 146.8, 145.8, 128.8, 128.4, 125.3, 117.7, 75.0, 52.9, 52.3, 51.2, 48.6, 47.8, 47.7, 43.5, 38.5, 36.0, 35.6, 35.0, 34.9, 34.0, 33.6, 32.9, 28.2, 27.4, 26.8, 25.4, 24.4, 24.4, 24.2, 21.9, 21.6, 20.6, 18.3, 18.2, 12.8.



1-(cyclohexylamino)-1-oxooctan-2-yl-3-oxotirucalla-7,24Z-dien-26-oate (**8d**). Yellow oil;  $R_f = 0.55$  (20% ethyl acetate in hexanes):  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 25 °C, TMS):  $\delta$  7.39

(m, 2H), 7.35 (m, 2H), 6.06 (bs, 1H), 6.03 (dt,  $J = 7.6, 1.6$  Hz, 1H), 5.97 (d,  $J = 2.6$  Hz, 1H), 5.30 (dd,  $J = 6.0, 3.2$  Hz, 1H), 3.83 (dtt,  $J = 10.4, 7.9, 4.1$  Hz, 1H), 2.77 (td,  $J = 14.5, 5.4$  Hz, 1H), 2.59 (m, 1H), 2.45 (m, 1H), 2.28 (dt,  $J = 14.1, 3.8$ , 1H), 2.25 (m, 1H), 2.10 (m, 2H), 1.99 (m, 2H), 1.97 (m, 1H), 1.98 (d,  $J = 1.6$  Hz, 3H), 1.93 (m, 4H), 1.82 (m, 1H), 1.76 (m, 2H), 1.73 (t,  $J = 8.7$  Hz, 1H), 1.69 (m, 2H), 1.64 (m, 1H), 1.56 (m, 2H), 1.53 (m, 2H), 1.49 (m, 1H), 1.48 (m, 2H), 1.48 (m, 1H), 1.47 (m, 2H), 1.40 (m, 1H), 1.36 (s, 9H), 1.31 (m, 2H), 1.29 (m, 2H), 1.28 (m, 1H), 1.26 (m, 2H), 1.18 (m, 4H), 1.16 (m, 1H), 1.11 (s, 3H), 1.05 (s, 3H), 1.01 (s, 3H), 1.00 (s, 3H), 0.89 (d,  $J = 6.2$  Hz, 3H), 0.88 (t,  $J = 6.7$  Hz, 3H) 0.81 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  216.9, 166.3, 165.8, 146.7, 145.9, 125.3, 117.8, 74.0, 52.9, 52.3, 51.2, 48.5, 47.8, 47.8, 43.4, 38.5, 36.1, 35.5, 35.0, 34.9, 34.0, 33.6, 32.9, 31.7, 31.6, 28.9, 28.2, 27.4, 26.9, 25.4, 24.6, 24.4, 24.5, 24.3, 22.5, 21.9, 21.6, 20.6, 18.4, 18.3, 14.0, 12.8.

#### 4. Conclusions

Herein we developed an efficient and versatile IMCR of Passerini for the functionalization of natural products like triterpenoids. It is important to highlight that alternative solvents can be used for improving the greenness of the Passerini reaction. Aliphatic and deactivated aromatic aldehydes led to the best results in our study, as was expected. Finally, it should be highlighted that the source of the used triterpenoid was sustainable and was obtained without causing harm to the plant and its environment.

**Author Contributions:** Conceptualization, R.G.-M. and H.A.G.-G.; methodology, F.R.-L. and E.G.R.-G.; software, F.R.-L.; validation, R.G.-M., F.R.-L. and R.G.-M.; formal analysis, R.G.-M.; investigation, F.R.-L. and R.G.-M.; resources, R.G.-M.; data curation, F.R.-L.; writing—original draft preparation, F.R.-L.; writing—review and editing, R.G.-M.; visualization, R.G.-M.; supervision, R.G.-M. and H.A.G.-G.; project administration, R.G.-M.; funding acquisition, R.G.-M. and H.A.G.-G. All authors have read and agreed to the published version of the manuscript.

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**Conflicts of Interest:** The authors declare no conflicts of interest.

#### References

1. Springob, K.; Kutchan, T.M. Introduction to the different classes of natural products. In *Plant-Derived Natural Products*; Osbourn, A., Lanzotti, V., Eds.; Springer: New York, NY, USA, 2009; pp. 3–50.
2. Talapatra, S.K.; Talapatra, B. Introduction: Enzymes. Cofactors/Coenzymes. Primary and Secondary Metabolites. Natural Products and their Functions. Plant Chemical Ecology. Biosynthesis. Metabolic Pathways. In *Chemistry of Plant Natural Products*; Springer: Berlin/Heidelberg, Germany, 2015; pp. 1–22.
3. Brahmshatriya, P.P.; Brahmshatriya, P.S. Terpenes: Chemistry, Biological Role, and Therapeutic Applications. In *Natural Products*; Ramawat, K., Mérillon, J.M., Eds.; Springer: Berlin/Heidelberg, Germany, 2013; pp. 2665–2691.
4. Rascón-Valenzuela, L.A.; Torres-Moreno, H.; Velázquez-Contreras, C.; Garibay-Escobar, A.; Robles-Zepeda, R.E. Triterpenoids: Synthesis, Uses in Cancer Treatment and Other Biological Activities. In *Advances in Medicine and Biology*; Berhardt, L.V., Ed.; Nova Science Publishers: New York, NY, USA, 2017; Volume 106, pp. 139–182.
5. Chudzik, M.; Korzonek-Szlacheta, I.; Król, W. Triterpenes as Potentially Cytotoxic Compounds. *Molecules* **2015**, *20*, 1610–1625. [[CrossRef](#)] [[PubMed](#)]
6. Morais, T.; da Costa-Silva, T.; Tempone, A.; Borborema, S.; Scotti, M.; de Sousa, R.; Araujo, A.; de Oliveira, A.; de Morais, S.; Sartorelli, P.; et al. Antiparasitic Activity of Natural and Semi-Synthetic Tirucallane Triterpenoids from *Schinus terebinthifolius* (Anacardiaceae): Structure/Activity Relationships. *Molecules* **2014**, *19*, 5761–5776. [[CrossRef](#)] [[PubMed](#)]

7. Sánchez-Monroy, M.; Jacobo-Herrera, N.; Zentella-Dehesa, A.; Hernández-Téllez, B.; Martínez-Vázquez, M. Masticadienonic and 3 $\alpha$ -OH Masticadienoic Acids Induce Apoptosis and Inhibit Cell Proliferation and Tumor Growth in Prostate Cancer Xenografts in Vivo. *Molecules* **2017**, *22*, 1479. [[CrossRef](#)] [[PubMed](#)]
8. Oviedo-Chavez, I.; Ramirez-Apan, T.; Martinez-Vazquez, M. Cytotoxic Activity and Effect on Nitric Oxide Production of Tirucallane-Type Triterpenes. *J. Pharm. Pharmacol.* **2005**, *57*, 1087–1091. [[CrossRef](#)] [[PubMed](#)]
9. Dzubak, P.; Hajduch, M.; Vydra, D.; Hustova, A.; Kvasnica, M.; Biedermann, D.; Markova, L.; Urban, M.; Sarek, J. Pharmacological Activities of Natural Triterpenoids and Their Therapeutic Implications. *Nat. Prod. Rep.* **2006**, *23*, 394–411. [[CrossRef](#)] [[PubMed](#)]
10. Tietze, L.F.F.; Brasche, G.; Gericke, K.M. Multicomponent reactions. In *Domino Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2006.
11. Dömling, A.E.; AlQahtani, A.D. General Introduction to MCRs: Past, Present, and Future. In *Multicomponent Reactions in Organic Synthesis*; Zhu, J., Wang, Q., Wang, M., Eds.; Wiley-VCH: Weinheim, Germany, 2015.
12. Wahby, Y.; Abdel-Hamid, H.; Salah Ayoup, M. Two decades of recent advances of Passerini reactions: Synthetic and potential pharmaceutical applications. *New J. Chem.* **2022**, *46*, 1445. [[CrossRef](#)]
13. Fouad, M.A.; Abdel-Hamid, H.; Ayoup, M.S. Two Decades of Recent Advances of Ugi Reactions: Synthetic and Pharmaceutical Applications. *RSC Adv.* **2020**, *10*, 42644–42681. [[CrossRef](#)] [[PubMed](#)]
14. Rudick, J.G.G.; Shaabani, S.; Dömling, A. Isocyanide-based multicomponent reactions. *Front. Chem.* **2020**, *7*, 918. [[CrossRef](#)] [[PubMed](#)]
15. Răzvan, C.; Ruijter, C.; Orru, R.V. Multicomponent Reactions: Advanced Tools for Sustainable Organic Synthesis. *Green Chem.* **2014**, *16*, 2958–2975.
16. Reguera, L.; Attorresi, C.I.; Ramírez, J.A.; Rivera, D.G. Steroid Diversification by Multicomponent Reactions. *Beilstein J. Org. Chem.* **2019**, *15*, 1236–1256. [[CrossRef](#)] [[PubMed](#)]
17. Gurrapu, S.; Walsh, W.J.; Brooks, J.M.; Jonnalagadda, S.C.; Mereddy, V.R. Synthesis of Lupane Triterpenoid Derivatives. *Nat. Prod. Indian J.* **2012**, *8*, 115–120.
18. Wiemann, J.; Heller, L.; Csuk, R. An Access to a Library of Novel Triterpene Derivatives with a Promising Pharmacological Potential by Ugi and Passerini Multicomponent Reactions. *Eur. J. Med. Chem.* **2018**, *150*, 176–194. [[CrossRef](#)] [[PubMed](#)]
19. Sommerwerk, S.; Heller, L.; Kuhfs, J.; Csuk, R. Selective Killing of Cancer Cells with Triterpenoic Acid Amides—The Substantial Role of an Aromatic Moiety Alignment. *Eur. J. Med. Chem.* **2016**, *122*, 452–464. [[CrossRef](#)] [[PubMed](#)]

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