molbank

MDPI

Communication

Synthesis of 5-Aroyl-2-aryl-3-hydroxypyridin-4(1*H*)-ones

Elena V. Steparuk, Dmitrii L. Obydennov * and Vyacheslav Y. Sosnovskikh

Institute of Natural Sciences and Mathematics, Ural Federal University, 51 Lenina ave., Ekaterinburg 620000, Russia; len079@yandex.ru (E.V.S.); vy.sosnovskikh@urfu.ru (V.Y.S.)
* Correspondence: dobydennov@mail.ru

Abstract: A two-stage synthesis of 5-aroyl-2-aryl-3-hydroxypyridin-4(1*H*)-ones (56–66% overall yields) was carried out by refluxing 5-aroyl-3-(benzyloxy)-2-(het)aryl-4*H*-pyran-4-ones with ammonium acetate in AcOH and subsequent debenzylation. The prepared *N*-unsubstituted 4-pyridones exist in the pyridone tautomeric form.

Keywords: 3-hydroxy-4-pyridones; 4-pyrones; debenzylation; metalloenzyme inhibitors; chelating agents; tautomerism

1. Introduction

3-Hydroxy-4-pyridones (3,4-HPOs) are well-known bidentate chelation agents for many metals [1–3]. The first marketed drug possessing a 3,4-HPO scaffold, deferiprone (Ferriprox), is an iron chelating agent for treating thalassemia approved in 1999 (Figure 1). Since the pyridine ring offers great possibilities for functionalization, a number of new 3,4-HPO-based polydentate chelators [2,4] and also 3,4-HPO-grafted fabrics for filtering uranium from wastewater [5] were developed afterward. Moreover, there are some natural examples of 3,4-HPOs, such as rubrifacine [6] and mimosine (leucenol), an amitotic agent first isolated from *Mimosa pudica* [7].

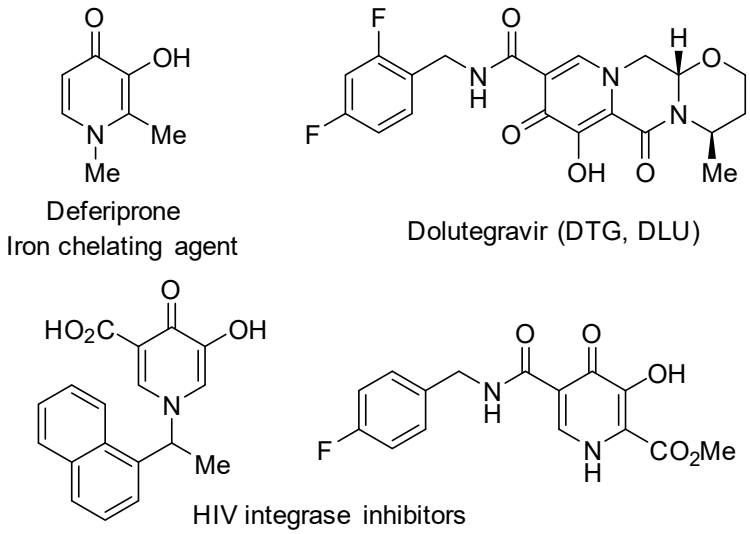


Figure 1. Some important 3-hydroxy-4-pyridones.

Additionally, 3-hydroxy-4-pyridones have recently received considerable attention as promising metal-binding pharmacophores, such as inhibitors of metalloenzymes, and thus are being now intensively investigated to design novel drugs, including antiviral ones [8]. As a result, approved HIV integrase strand transfer inhibitors (INSTI) dolutegravir, bictegravir, and cabotegravir, as well as several newly developed drug candidates (Figure 1),

check for updates

Citation: Steparuk, E.V.; Obydennov, D.L.; Sosnovskikh, V.Y. Synthesis of 5-Aroyl-2-aryl-3-hydroxypyridin-4(1*H*)-ones. *Molbank* **2023**, *2023*, M1668. https://doi.org/10.3390/M1668

Academic Editor: Fawaz Aldabbagh

Received: 18 May 2023
Revised: 6 June 2023
Accepted: 8 June 2023
Published: 10 June 2023

possess a 3,4-HPO structural motif designed to coordinate magnesium ions of HIV integrase and thus prevent integration of the viral DNA [9–15]. Additionally, the inhibitors of catechol-*O*-methyltransferase (contains Mg^{2+}) [16], human cytomegalovirus pUL89 protein (Mn^{2+}) [17], and influenza cap-dependent endonuclease (Mn^{2+}) [18] were discovered.

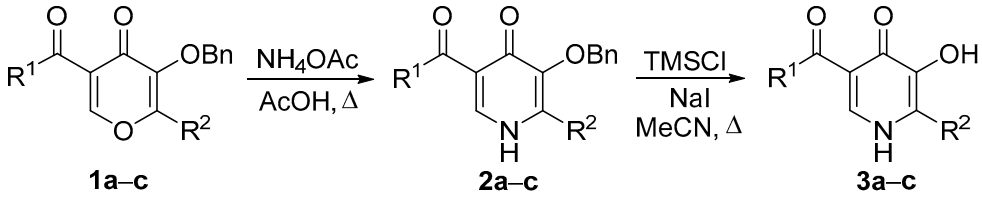
However, methods for preparing 3,4-HPOs can dramatically differ depending on the substituent location and type and may require multi-stage synthetic schemes with restricted reaction scope [12,19]. For some of them, there is still no efficient synthetic approach.

In this article, we focused our attention on the synthesis of hitherto unknown *N*-unsubstituted 5-aroyl-2-(het)aryl-3-hydroxypyridin-4(1*H*)-ones.

2. Results and Discussion

Recently, we synthesized a series of 5-aroyl-3-(benzyloxy)-2-(het)aryl-4*H*-pyran-4-ones **1** by acylation of enaminodiones with acylbenzotriazoles *via* soft enolization [20]. To the best of our knowledge, no examples of *N*-unsubstituted 3,4-HPOs **3** bearing 2-(het)aryl and 5-aroyl substituents have been described in the literature to date. Therefore, we decided to employ the ANRORC reaction of pyrones **1a–c** with ammonia to synthesize pyridones **2a–c** and then reach desired 3-hydroxy-4-pyridones **3** by the debenzylation of the latter.

We found that pyrones **1a–c** on heating at 100 °C for 3 h with ammonium acetate in glacial AcOH afforded corresponding pyridones **2a–c** in 61–72% yields (Scheme 1, Table 1). Subsequent dilution with water and recrystallization from toluene made it possible to isolate the products in pure form. In the reaction with ethanolic ammonia solution, however, it turned out that two equivalents of ammonia were involved, and [4-amino-5-(benzyloxy)-6-phenylpyridin-3-yl](phenyl)methanone was obtained from the corresponding pyrone [20]. Additionally, no reaction appeared when pyrones **1** were refluxed in an ethanolic solution of ammonium chloride. The reaction mechanism includes the attack of the ammonia molecule at the C-6 position, followed by the pyrone ring opening and intramolecular cyclization [21].



Scheme 1. Synthesis of pyridones **2** and 3,4-HPOs **3**.

Table 1. Yields of products **2** and **3**.

Entry	Compounds 1–3	R^1	R^2	Yield of 2	Yield of 3
1	**a**	Ph	furan-2-yl	68	89
2	**b**	4-ClC_6H_4	furan-2-yl	72	92
3	**c**	4-ClC_6H_4	Ph	61	92

The debenzylation of products **2a–c** under the action of TMSI generated in situ in anhydrous acetonitrile from TMSCl and NaI allowed us to obtain 5-acyl-2-hetaryl substituted 3,4-HPOs **3a–c** in 89–92% yields. It is important to note that the purification of products **3** did not require chromatography and could be achieved by simple recrystallization.

The structures of all synthesized compounds were characterized based on ^1H, ^{13}C NMR (see SM), and IR spectroscopy data and supported by HRMS values. Although *N*-unsubstituted pyridones can undergo pyridinol/pyridone tautomerism [22,23], compounds **2** and **3** exist in the pyridone form. The ^1H NMR spectra of these compounds display the presence of the characteristic pyridone H-6 singlet or doublet ($J_{H\text{-}6,NH}$ = 3.6–6.6 Hz) at δ 7.78–7.90 ppm and the downfield singlet or doublet of the NH group at δ 12.14–12.30 ppm. The ^{13}C NMR spectra show the characteristic peaks of the acyl moiety and the pyridone

carbonyl group at δ 192.6–194.1 and 168.6–171.6 ppm, respectively. For compound **2**, the NMR signals of the aliphatic methylene group appeared at δ 5.03–5.30 ppm (^{1}H NMR) and 71.5–72.1 ppm (^{13}C NMR).

In summary, we described a convenient two-step way (starting from pyrones) for synthesizing new 5-aroyl-2-(het)aryl-3-hydroxypyridin-4(1*H*)-ones in 56–66% overall yields. This will expand the design possibilities in the search for new inhibitors of metalloenzymes with antiviral activity.

3. Materials and Methods

NMR spectra were recorded on Bruker Avance III-500 (^{1}H—500 MHz and ^{13}C—126 MHz) spectrometers (Bruker BioSpin GmbH, Rheinstetten, Germany) in DMSO-d_6. Chemical shifts are reported relative to TMS as an internal standard in ppm, and *J* values are given in Hz. IR spectra were recorded on a Shimadzu IRSpirit-T (QATR-S) instrument (FTIR mode, diamond crystal, Shimadzu Corp., Kyoto, Japan). The mass spectra (ESI-MS) were measured with a Waters Xevo QTof instrument (Waters Corp., Milford, MA, USA). All solvents used were dried and distilled per standard procedures. Melting points were determined on a Stuart SMP40 apparatus. Pyrones **1a–c** were prepared according to the literature data [20].

3.1. General Procedure for the Synthesis of 3-Benzyloxypyridin-4(1H)-ones **2**

Pyrone **1** (0.27 mmol) was dissolved in glacial AcOH, and NH_4OAc (83.2 mg, 1.08 mmol) was added. The resulting mixture was stirred at 100 °C for 3 h, and then excess water was added. The precipitate formed was filtered and recrystallized from toluene.

5-Benzoyl-3-(benzyloxy)-2-(furan-2-yl)pyridin-4(1H)-one (**2a**). Brown solid (68 mg, 68%), mp 190–191 °C. IR (ATR) ν 2879, 2854, 1655, 1614, 1540, 1314, 1255, 1188, 999, and 743 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.30 (s, 2H, CH_2), 6.74 (dd, *J* = 3.4, *J* = 1.7, 1H, H-4 furan), 7.17 (d, *J* = 3.4, 1H, H-3 furan), 7.31–7.39 (m, 3H, Ph), 7.41 (d, *J* = 7.0, 2H, H-2, H-6 Ph), 7.50 (t, *J* = 7.7, 2H, H-3, H-5 Ph), 7.61 (t, *J* = 7.4, 1H, H-4 Ph), 7.72 (d, *J* = 7.2, 2H, H-2, H-6 Ph), 7.79 (s, 1H, H-6 pyridone), 8.01 (d, *J* = 1.0, 1H, H-5 furan), and 12.14 (s, 1H, NH). ^{13}C NMR (126 MHz, DMSO-d_6) δ 71.5 (CH_2), 112.9, 114.1, 125.3, 126.4, 128.1, 128.16, 128.2, 128.6, 128.9, 129.1, 129.6, 132.7, 137.0, 137.6, 143.6, 144.6, 171.2 (C=O), and 194.1 (C=O). HRMS (ESI): calculated for $C_{23}H_{18}NO_4$ $[M + H]^+$ 372.1236, found 372.1249.

3-(Benzyloxy)-5-(4-chlorobenzoyl)-2-(furan-2-yl)pyridin-4(1H)-one (**2b**). Brown solid (79 mg, 72%), mp 194–195 °C. IR (ATR) ν 2779, 2682, 1647, 1616, 1536, 1191, 1008, and 794 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.28 (s, 2H, CH_2), 6.75 (dd, *J* = 3.4, *J* = 1.8, 1H, H-4 furan), 7.16 (d, *J* = 3.4, 1H, H-3 furan), 7.33 (tt, *J* = 7.2, *J* = 1.4, 1H, H-4 Ph), 7.37 (t, *J* = 7.2, 2H, H-3, H-5 Ph), 7.41 (d, *J* = 7.0, 2H, H-2, H-6 Ph), 7.56 (d, *J* = 8.5, 2H, H-3, H-5 Ar), 7.72 (d, *J* = 8.5, 2H, H-2, H-6 Ar), 7.83 (s, 1H, H-6 pyridone), 8.01 (d, *J* = 1.0, 1H, H-5 furan), and 12.21 (s, 1H, NH). ^{13}C NMR (126 MHz, DMSO-d_6) δ 71.6 (CH_2), 112.9, 114.1, 125.7, 128.1, 128.2, 128.2, 128.5, 130.9, 136.4, 137.0, 137.4, 138.2, 143.5, 143.7, 144.6, 171.2 (C=O), and 193.0 (C=O). HRMS (ESI): calculated for $C_{23}H_{17}ClNO_4$ $[M + H]^+$ 406.0846, found 406.0853.

3-(Benzyloxy)-5-(4-chlorobenzoyl)-2-phenylpyridin-4(1H)-one (**2c**). Brown solid (68 mg, 61%), mp 160–161 °C. IR (ATR) ν 3019, 2866, 1657, 1613, 1535, 1190, and 752 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.03 (s, 2H, CH_2), 7.10–7.19 (m, 2H, Ph), 7.21–7.26 (m, 3H, Ph), 7.49–7.53 (m, 3H, Ph), 7.54–7.57 (m, 2H, Ph), 7.58 (d, *J* = 8.5, 2H, H-3, H-5 Ar), 7.77 (d, *J* = 8.5, 2H, H-2, H-6 Ar), 7.90 (d, *J* = 6.2, 1H, H-6 pyridone), and 12.18 (d, *J* = 6.2, 1H, NH). ^{13}C NMR (126 MHz, DMSO-d_6) δ 72.1 (CH_2), 126.5, 127.7, 128.0, 128.1, 128.25, 128.33, 129.0, 129.6, 131.0, 136.4, 137.1, 138.0, 140.3, 145.5, 171.6 (C=O), and 193.3 (C=O). HRMS (ESI): calculated for $C_{25}H_{18}ClNO_3$ $[M + H]^+$ 416.1053, found 416.1042.

3.2. General Procedure for the Synthesis of 3-Hydroxypyridin-4(1H)-ones **3**

Corresponding pyridone **2** (0.25 mmol) and NaI (69 mg, 0.37 mmol) were dissolved in anhydrous MeCN (3 mL), and Me_3SiCl (53 mg, 0.49 mmol) was added. The solution

was stirred at 80 °C for 1.5 h (TLC monitoring). Then, water (4 mL) was added, and the precipitated product was filtered and recrystallized from toluene.

5-Benzoyl-2-(furan-2-yl)-3-hydroxypyridin-4(1H)-one (**3a**). Brown solid (63 mg, 89%), mp 234–235 °C. IR (ATR) ν 3334, 3054, 1600, 1482, 1233, and 746 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ 6.77 (dd, J = 3.3, J = 1.3, 1H, H-4 furan), 7.13 (d, J = 3.3, 1H, H-3 furan), 7.46 (t, J = 7.6, 2H, H-3, H-5 Ph), 7.59 (t, J = 7.3, 1H, H-4 Ph), 7.75 (d, J = 7.5, 2H, H-2, H-6 Ph), 7.78 (d, J = 3.6, 1H, H-6 pyridone), 7.99 (s, 1H, H-5 furan), and 12.24 (s, 1H, NH); the OH proton was not observed. ^{13}C NMR (126 MHz, DMSO-d_6) δ 112.5, 112.8, 119.2, 121.2, 128.0, 129.2, 132.4, 136.6, 137.9, 143.8, 144.1, 144.5, 168.6 (C=O), and 193.7 (C=O). HRMS (ESI): calculated for $C_{16}H_{12}NO_4$ $[M + H]^+$ 282.0766, found 282.0764.

5-(4-Chlorobenzoyl)-2-(furan-2-yl)-3-hydroxypyridin-4(1H)-one (**3b**). Brown solid (72 mg, 92%), mp 298–299 °C. IR (ATR) ν 3311, 3060, 2958, 1648, 1523, 1405, 1273, and 736 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ 6.77 (dd, J = 3.1, J = 1.6, 1H, H-4 furan), 7.13 (d, J = 3.3, 1H, H-3 furan), 7.53 (d, J = 8.4, 2H, H-3, H-5 Ar), 7.75 (d, J = 8.4, 2H, H-2, H-6 Ar), 7.81 (d, J = 6.6, 1H, H-6 pyridone), 7.99 (s, 1H, H-5 furan), and 12.30 (d, J = 6.6, 1H, NH); the OH proton was not observed. ^{13}C NMR (126 MHz, DMSO-d_6) δ 112.6, 112.9, 119.3, 120.8, 128.1, 131.1, 136.7, 137.0, 137.2, 143.8, 144.1, 144.7, 168.7 (C=O), and 192.6 (C=O). HRMS (ESI): calculated for $C_{16}H_{10}ClNO_4$ $[M + H]^+$ 316.0377, found 316.0376.

5-(4-Chlorobenzoyl)-3-hydroxy-2-phenylpyridin-4(1H)-one (**3c**). Brown solid (75 mg, 92%), mp 292–293 °C. IR (ATR) ν 3234, 3070, 1641, 1594, 1379, 1263, 1087, and 752 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ 7.48 (tt, J = 7.3, J = 1.2, 1H, H-4 Ph), 7.52–7.57 (m, 4H, Ph, Ar), 7.75–7.79 (m, 4H, Ar, Ph), 7.88 (d, J = 6.1, 1H, H-6 pyridone), 8.40–9.40 (br s, 1H, OH), and 12.22 (d, J = 6.1, 1H, NH). ^{13}C NMR (126 MHz, DMSO-d_6) δ 120.8, 127.4, 128.1, 128.40, 128.43, 129.1, 131.16, 131.19, 136.6, 136.9, 137.3, 146.1, 169.0 (C=O), and 192.7 (C=O). HRMS (ESI): calculated for $C_{18}H_{12}ClNO_3$ $[M + H]^+$ 326.0584, found 326.0599.

Supplementary Materials: The following supporting information can be downloaded online: Full ^1H and ^{13}C NMR spectra of all synthesized compounds.

Author Contributions: Conceptualization and methodology were provided by V.Y.S. and D.L.O.; E.V.S. conceived and designed the experiments.; the experimental work was conducted by E.V.S.; D.L.O. and E.V.S. analyzed the results; E.V.S. studied and systemized the spectral data; project administration and funding acquisition were carried out by V.Y.S. and D.L.O. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Russian Science Foundation, grant number 22-73-10236 (https://rscf.ru/project/22-73-10236/ (accessed on 24 April 2023)).

Data Availability Statement: Data is contained within the article and Supplementary Materials.

Acknowledgments: Analytical studies were carried out using equipment at the Center for Joint Use 'Spectroscopy and Analysis of Organic Compounds' at the Postovsky Institute of Organic Synthesis of the Russian Academy of Sciences (Ural Branch) and the Laboratory of Complex Investigations and Expert Evaluation of Organic Materials of the Center for Joint Use at the Ural Federal University.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Santos, M.A.; Marques, S.M.; Chaves, S. Hydroxypyridinones as "Privileged" Chelating Structures for the Design of Medicinal Drugs. *Coord. Chem. Rev.* **2012**, *256*, 240–259. [CrossRef]
2. Santos, M.A.; Irto, A.; Buglyó, P.; Chaves, S. Hydroxypyridinone-Based Metal Chelators towards Ecotoxicity: Remediation and Biological Mechanisms. *Molecules* **2022**, *27*, 1966. [CrossRef] [PubMed]
3. Zhou, D.; Tian, Y.; Ma, Y. Preparation of 5-Functionalised Pyridine Derivatives Using a Br/Mg Exchange Reaction: Application to the Synthesis of an Iron-Chelator Prodrug. *J. Chem. Res.* **2017**, *41*, 627–630. [CrossRef]
4. Zhou, X.; Dong, L.; Shen, L. Hydroxypyridinones as a very Promising Platform for Targeted Diagnostic and Therapeutic Radiopharmaceuticals. *Molecules* **2021**, *26*, 6997. [CrossRef] [PubMed]

5. Zhang, M.; Yuan, M.; Zhang, M.; Wang, M.; Chen, J.; Li, R.; Qiu, L.; Feng, X.; Hu, J.; Wu, G. Efficient Removal of Uranium from Diluted Aqueous Solution with Hydroxypyridone Functionalized Polyethylene Nonwoven Fabrics. *Radiat. Phys. Chem.* **2020**, *171*, 108742. [CrossRef]
6. Feistner, G.; Budzikiewicz, H. On the Structure of Rubrifacine. *Can. J. Chem.* **1985**, *63*, 495–499. [CrossRef]
7. Adams, R.; Cristol, S.J.; Anderson, A.A.; Albert, A.A. The Structure of Leucenol. I. *J. Am. Chem. Soc.* **1945**, *67*, 89–92. [CrossRef]
8. Chen, A.Y.; Adamek, R.N.; Dick, B.L.; Credille, C.V.; Morrison, C.N.; Cohen, S.M. Targeting Metalloenzymes for Therapeutic Intervention. *Chem. Rev.* **2019**, *119*, 1323–1455. [CrossRef] [PubMed]
9. Ji, M.; Lazerwith, S.E.; Pyun, H.-J. Polycyclic-Carbamoylpyridone Compounds and Their Pharmaceutical Use. U.S. Patent US9700554, 11 July 2017.
10. Miyazaki, S.; Isoshima, H.; Oshita, K.; Kawashita, S.; Nagahashi, N.; Terashita, M. Substituted Spiropyrido[1,2-a]Pyrazine Derivative and Medicinal Use Thereof as HIV Integrase Inhibitor. U.S. Patent US10087178, 2 October 2018.
11. Kankanala, J.; Kirby, K.A.; Liu, F.; Miller, L.; Nagy, E.; Wilson, D.J.; Parniak, M.A.; Sarafianos, S.G.; Wang, Z. Design, Synthesis, and Biological Evaluations of Hydroxypyridonecarboxylic Acids as Inhibitors of HIV Reverse Transcriptase Associated RNase H. *J. Med. Chem.* **2016**, *59*, 5051–5062. [CrossRef] [PubMed]
12. Kawasuji, T.; Johns, B.A.; Yoshida, H.; Taishi, T.; Taoda, Y.; Murai, H.; Kiyama, R.; Fuji, M.; Yoshinaga, T.; Seki, T.; et al. Carbamoyl Pyridone HIV-1 Integrase Inhibitors. 1. Molecular Design and Establishment of an Advanced Two-Metal Binding Pharmacophore. *J. Med. Chem.* **2012**, *55*, 8735–8744. [CrossRef] [PubMed]
13. Rostami, M.; Sirous, H.; Zabihollahi, R.; Aghasadeghi, M.R.; Sadat, S.M.; Namazi, R.; Saghaie, L.; Memarian, H.R.; Fassihi, A. Design, Synthesis and Anti-HIV-1 Evaluation of a Series of 5-Hydroxypyridine-4-One Derivatives as Possible Integrase Inhibitors. *Med. Chem. Res.* **2015**, *24*, 4113–4127. [CrossRef]
14. Sayyed, S.K.; Quraishi, M.; Jobby, R.; Rameshkumar, N.; Kayalvizhi, N.; Krishnan, M.; Sonawane, T. A Computational Overview of Integrase Strand Transfer Inhibitors (INSTIs) against Emerging and Evolving Drug-Resistant HIV-1 Integrase Mutants. *Arch. Microbiol.* **2023**, *205*, 142. [CrossRef] [PubMed]
15. Sirous, H.; Fassihi, A.; Brogi, S.; Campiani, G.; Christ, F.; Debyser, Z.; Gemma, S.; Butini, S.; Chemi, G.; Grillo, A.; et al. Synthesis, Molecular Modelling and Biological Studies of 3-Hydroxypyrane-4-One and 3-Hydroxy-Pyridine-4-One Derivatives as HIV-1 Integrase Inhibitors. *Med. Chem.* **2019**, *15*, 755–770. [CrossRef] [PubMed]
16. De Beer, J.; Petzer, J.P.; Lourens, A.C.U.; Petzer, A. Design, Synthesis and Evaluation of 3-Hydroxypyridin-4-Ones as Inhibitors of Catechol-O-Methyltransferase. *Mol. Divers.* **2021**, *25*, 753–762. [CrossRef] [PubMed]
17. Senaweera, S.; Edwards, T.C.; Kankanala, J.; Wang, Y.; Sahani, R.L.; Xie, J.; Geraghty, R.J.; Wang, Z. Discovery of N-Benzyl Hydroxypyridone Carboxamides as a Novel and Potent Antiviral Chemotype against Human Cytomegalovirus (HCMV). *Acta Pharm. Sin. B* **2022**, *12*, 1671–1684. [CrossRef] [PubMed]
18. Fujishita, T.; Mikamiyama, M.; Kawai, M.; Akiyama, T. Substituted 3-Hydroxy-4-Pyridone Derivative. U.S. Patent US8835461, 16 September 2014.
19. Ma, Y.; Hider, R.C. Novel Synthetic Approach to Fluoro- and Amido-Disubstituted 3-Hydroxypyridin-4-Ones. *J. Fluor. Chem.* **2015**, *173*, 29–34. [CrossRef]
20. Obydennov, D.L.; Viktorova, V.V.; Chernyshova, E.V.; Shirinkin, A.S.; Usachev, S.A.; Sosnovskikh, V.Y. Direct Synthesis of 5-Acyl-3-Oxy-4-Pyrones Based On Acid-Catalyzed Acylation of Enaminodiones with Acylbenzotriazoles via Soft Enolization. *Synthesis* **2020**, *52*, 2267–2276. [CrossRef]
21. Obydennov, D.L.; Khammatova, L.R.; Steben'kov, V.D.; Sosnovskikh, V.Y. Synthesis of novel polycarbonyl Schiff bases by ring-opening reaction of ethyl 5-acyl-4-pyrone-2-carboxylates with primary mono- and diamines. *RSC Advances* **2019**, *9*, 40072–40083. [CrossRef] [PubMed]
22. Obydennov, D.L.; Simbirtseva, A.E.; Piksin, S.E.; Sosnovskikh, V.Y. 2,6-Dicyano-4-pyrone as a Novel and Multifarious Building Block for the Synthesis of 2,6-Bis(hetaryl)-4-pyrones and 2,6-Bis(hetaryl)-4-pyridinols. *ACS Omega* **2020**, *5*, 33406–33420. [CrossRef] [PubMed]
23. Usachev, S.A.; Nigamatova, D.I.; Mysik, D.K.; Naumov, N.A.; Obydennov, D.L.; Sosnovskikh, V.Y. 2-Aryl-6-Polyfluoroalkyl-4-Pyrones as Promising R^F-Building-Blocks: Synthesis and Application for Construction of Fluorinated Azaheterocycles. *Molecules* **2021**, *26*, 4415. [CrossRef] [PubMed]