catalysts

MDPI

Article

Depolymerization of P4HB and PBS Waste and Synthesis of the Anticancer Drug Busulfan from Plastic Waste

Daniel L. Lourenço and Ana C. Fernandes *

Centro de Química Estrutural, Institute of Molecular Sciences, Departamento de Engenharia Química, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049-001 Lisboa, Portugal; daniellourenco98@hotmail.com

* Correspondence: anacristinafernandes@tecnico.ulisboa.pt; Tel.: +351-218419220

Abstract: Sustainable synthesis of pharmaceuticals is one of the main challenges for the pharmaceutical industry. Production of these compounds from plastic waste can provide an innovative and ecological approach to their sustainable synthesis. In this context, plastic waste can be regarded as a potential cheap resource for the production of compounds of interest to the pharmaceutical industry. In this work, the first methodologies for the reductive depolymerization of poly(4-hydroxybutyrate) (P4HB) and polybutylene succinate (PBS) plastic waste are reported using the catalyst systems $MoO_2Cl_2(H_2O)_2$/silane, $MoO_2Cl_2(H_2O)_2$/borane and KOH/$PhSiH_3$ with moderate to excellent yields. We also developed the first synthetic strategy for the synthesis of a drug, the anticancer busulfan, from P4HB and PBS plastic waste with moderate overall yields.

Keywords: plastic waste; poly(4-hydroxybutyrate); polybutylene succinate; reductive depolymerization; busulfan

Citation: Lourenço, D.L.; Fernandes, A.C. Depolymerization of P4HB and PBS Waste and Synthesis of the Anticancer Drug Busulfan from Plastic Waste. *Catalysts* **2022**, *12*, 381. https://doi.org/10.3390/catal12040381

Academic Editor: Kotohiro Nomura

Received: 25 February 2022
Accepted: 25 March 2022
Published: 29 March 2022

1. Introduction

Plastics have become ubiquitous materials in our daily life, and the world without plastics seems unimaginable today. Consequently, plastic pollution has increased drastically over the last century and is currently one of the biggest problems facing the planet. It is urgent to mitigate the environmental impact of plastics. To address this challenge, it is crucial to continue the development of new, cost-efficient and sustainable processes for the valorization of plastic waste. In the last years, great efforts have been made to develop new methodologies for the depolymerization of plastic waste into a value-added chemical to be used as raw materials in the chemical industry [1–15]. Among these methodologies, the reductive depolymerization [16] of polyester waste has attracted the attention of the scientific community using different catalysts and H_2, silanes and alcohols as the reducing agents [17–25].

Sustainable synthesis of biologically active and pharmaceutical compounds is one of the main challenges for the pharmaceutical industry and has been investigated mainly from biomass resources [26–32]. Plastic waste can also be regarded as a potential cheap resource for the production of biologically active compounds and pharmaceuticals. To the best of our knowledge, there is no example of the synthesis of a drug from plastic waste described in the literature. Most of the research on the valorization of plastic waste has been directed towards the synthesis of monomers and fuels [16–25].

Busulfan, 4-methylsulfonyloxybutyl methanesulfonate (Figure 1), is an antineoplastic in the class of alkylating agents, used to treat various forms of cancer since 1959. Busulfan has been used to treat chronic myelogenous leukemia and certain blood disorders, such as polycythemia vera and myeloid metaplasia, and it has also been applied in some conditioning regimens prior to bone marrow transplant [33–36].

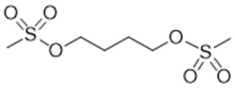


Figure 1. Structure of busulfan.

The search for new synthetic strategies for the production of anticancer drugs, which usually involves several reaction steps [37,38], in a sustainable way, continues to be a challenging topic for the pharmaceutical industry. In continuation of our research using oxo-complexes as efficient catalysts for the synthesis of organic compounds [39–43], in this work, we investigated the reductive depolymerization of P4HB and PBS plastic waste into 1,4-butanediol. We also developed the first synthesis of a pharmaceutical, the anticancer drug busulfan, from these plastic wastes.

2. Discussion and Results

In the first part of this work, we studied the reductive depolymerization of the two aliphatic polyesters poly(4-hydroxybutyrate) (P4HB) and polybutylene succinate (PBS), obtained from a non-infected commercial surgical suture (Figure 2a) and a Delta Q eQo coffee capsule, a Portuguese coffee (Figure 2b), respectively. To the best of our knowledge, there are no methodologies reported in the literature for the reductive depolymerization of these polyesters. The reductive depolymerization of P4HB was investigated using the catalytic system silane and $MoO_2Cl_2(H_2O)_2$, which employs different silanes as the reducing agents, including $PhSiH_3$, $(EtO)_2MeSiH$, PMHS (poly(methylhydrosiloxane)) and TMDS (1,1,3,3-tetramethyldisiloxane).

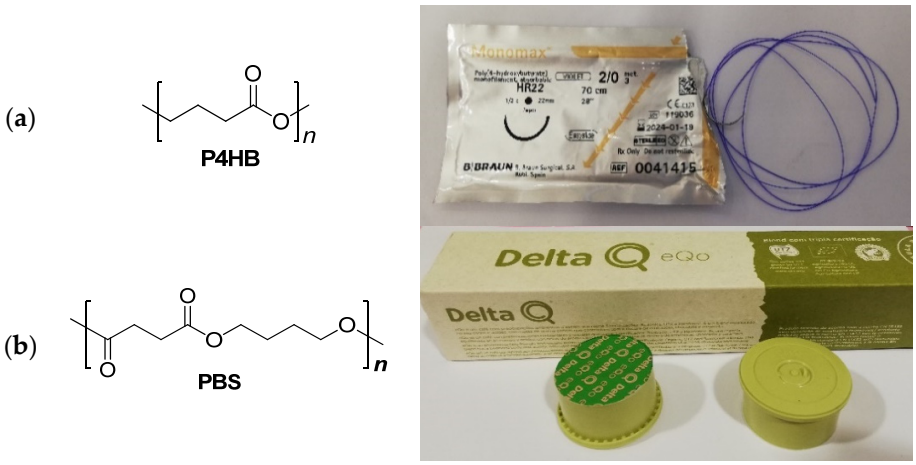
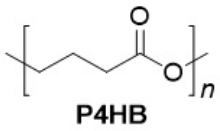
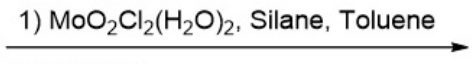


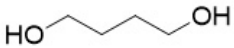
Figure 2. (**a**) Non-infected commercial surgical suture; (**b**) Delta Q eQo coffee capsules.

The reductive depolymerization of P4HB was initially carried out in the presence of 2 mol% of $MoO_2Cl_2(H_2O)_2$ using 1 or 3 equivalents of PMHS in toluene at reflux temperature for 24 h. These reactions led to the formation of 1,4-butanediol with 39% and 59% yields, respectively (Table 1, entries 1 and 2). When the reaction was carried out in the presence of 5 mol% of catalyst and 3 equiv. of PMHS, the yield of 1,4-butanediol increased slightly to 63% (Table 1, entry 3). The depolymerization of P4HB was also studied using $(EtO)_2MeSiH$ (3 equiv.) as the reducing agent and $MoO_2Cl_2(H_2O)_2$ (2 mol%) as the catalyst, producing 1,4-butanediol with 50% yield after 24 h at reflux temperature (Table 1, entry 4). This diol was also obtained in the 55% yield from the reaction of P4HB with $PhSiH_3$ (3 equiv.) in the presence of 5 mol% of $MoO_2Cl_2(H_2O)_2$ (Table 1, entry 5).

Table 1. Reductive depolymerization of P4HB with the catalytic system $MoO_2Cl_2(H_2O)_2$/Silane [a].







Entry	Catalyst (mol%)	Silane	Silane (Equiv.)	Temp. (°C)	Time (h)	Yield (%) [b]
1	2	PMHS	1	110	24	39
2	2	PMHS	3	110	24	59
3	5	PMHS	3	110	24	63
4	2	$(EtO)_2MeSiH$	3	110	24	50
5	5	$PhSiH_3$	3	110	24	55
6	5	TMDS	3	110	24	72
7	2	TMDS	2	110	24	52
8	2	TMDS	3	110	24	59
9	5	TMDS	2	110	24	52
10	5	TMDS	3	r. t.	48	No reaction
11	5	TMDS	3	110	24	65 [c]

[a] The reactions were carried out with 0.5 mmol of P4HB, obtained from a non-infected surgical suture. [b] Yields were determined by ^1H NMR using mesitylene as the internal standard. [c] The reaction was carried out using 2.0 mmol of P4HB.

To evaluate the efficiency of the catalytic system $MoO_2Cl_2(H_2O)_2$/TMDS in the depolymerization of P4HB, this reaction was explored using different amounts of $MoO_2Cl_2(H_2O)_2$ and TMDS in toluene at reflux and ambient temperatures. The best yield of 1,4-butanediol (72%, Figures S1 and S2) was observed in the presence of 5 mol% of $MoO_2Cl_2(H_2O)_2$ and 3 equivalents of TMDS after 24 h at reflux (Table 1, entry 6). When the depolymerization was carried out with smaller amounts of catalyst and TMDS, the diol was formed with yields of approximately 50% (Table 1, entries 7–9). At room temperature, the depolymerization of P4HB with the $MoO_2Cl_2(H_2O)_2$/TMDS system did not occur, demonstrating the effect of temperature on the depolymerization of P4HB (Table 1, entry 10).

To study the possible scale-up of this methodology, the depolymerization of P4HB was performed from 2 mmol (0.172 g) of this polyester with the catalytic system $MoO_2Cl_2(H_2O)_2$/TMDS, which also leads to the formation of 1,4-butanediol with good yield (65%) (Table 1, entry 11). This result is very interesting because it suggests the possible application of this cheap and environmentally friendly catalytic system to the large-scale production of 1,4-butanediol, which would contribute to reducing the use of fossil resources.

In this work, the possible use of the catalyst $MoO_2Cl_2(H_2O)_2$ (5 mol%) in several consecutive reductive depolymerizations of P4HB was also explored. This study was carried out in toluene at 110 °C by successive additions of P4HB and TMDS to the reaction mixture, without separating the catalyst at the end of each reaction. We concluded that the catalyst remained active during the eight reactions, by observing the complete reduction of P4HB and the formation of 1,4-butanediol in yields between 67% and 72% (Figure 3).

The reductive depolymerization of polyester PBS, obtained from Delta Q eQo coffee capsules cut into small pieces was also studied with the catalytic system $MoO_2Cl_2(H_2O)_2$/silane (Table 2). The depolymerization of PBS was initially investigated using PMHS as the reducing agent and $MoO_2Cl_2(H_2O)_2$ as the catalyst. The reaction performed with 5 mol% of catalyst and 2 equivalents of PMHS produced 1,4-butanediol with only 48% yield after 48 h (Table 2, entry 1). When this reaction was carried out using 6 equivalents of PMHS, this diol was obtained with 72% yield (Table 2, entry 2). Then, the depolymerization of PBS was studied using $PhSiH_3$ (6 equiv.) in the presence of 5 mol% of $MoO_2Cl_2(H_2O)_2$, producing 1,4-butanediol with 67% yield after 48 h at reflux temperature (Table 2, entry 3). The reductive depolymerization of PBS carried out with TMDS (6 equiv.) and 5 mol% of $MoO_2Cl_2(H_2O)_2$ led to the formation of 1,4-butanediol with the best yield (75%) after 48 h at reflux temperature (Table 2, entry 4), while using 4 equivalents of TMDS, 1,4-butanediol

was obtained with only 48% yield (Table 2, entry 5). In contrast, at room temperature, this reaction did not occur (Table 2, entry 6). Finally, we also successfully applied the catalytic system $MoO_2Cl_2(H_2O)_2$/TMDS to the depolymerization of 2.0 mmol (0.344 g) of PBS, obtaining 1,4-butanediol with 69% yield (Table 2, entry 7).

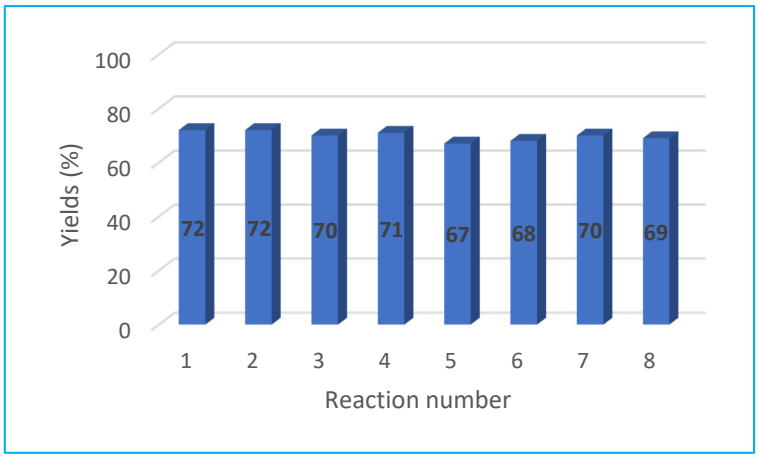
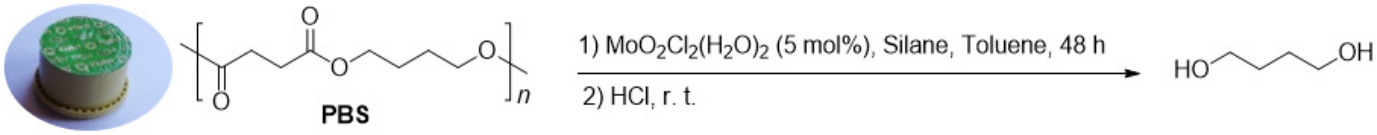


Figure 3. Use of $MoO_2Cl_2(H_2O)_2$ in consecutive reductive depolymerizations of P4HB. The reactions were carried out using $MoO_2Cl_2(H_2O)_2$ (5 mol%) by successive additions of P4HB (0.5 mmol) and TMDS (1.5 mmol) to the reaction mixture, without separating the catalyst at the end of each reaction. Yields were determined by ^{1}H NMR spectroscopy, using mesitylene as an internal standard.

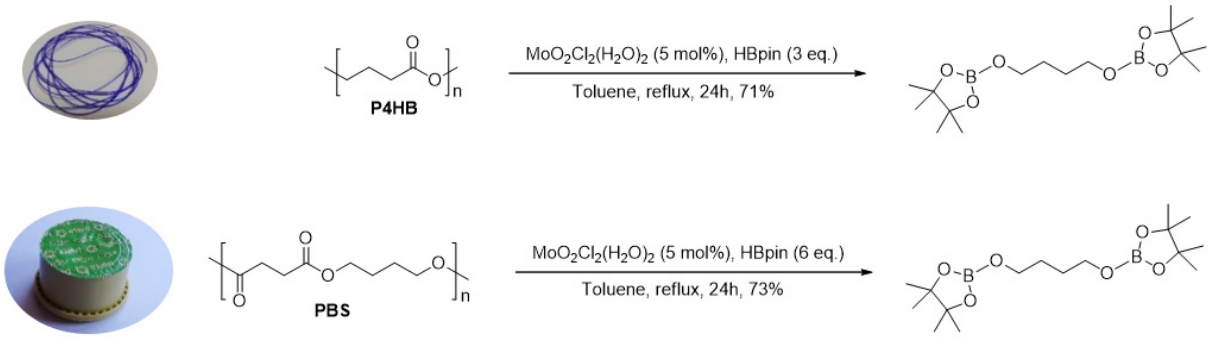
Table 2. Reductive depolymerization of PBS with the catalytic system $MoO_2Cl_2(H_2O)_2$/Silane [a].



Entry	Silane	Silane (Equiv.)	Temp. (°C)	Yield (%) [b]
1	PMHS	2	110	48
2	PMHS	6	110	72
3	$PhSiH_3$	6	110	67
4	TMDS	6	110	75
5	TMDS	4	110	48
6	TMDS	6	r. t.	No reaction
7	TMDS	6	110	69 [c]

[a] The reactions were carried out with 0.25 mmol of PBS, obtained from a Delta Q eQo coffee capsule. [b] Yields were determined by ^{1}H NMR using mesitylene as the internal standard. [c] The reaction was carried out using 2.0 mmol of PBS.

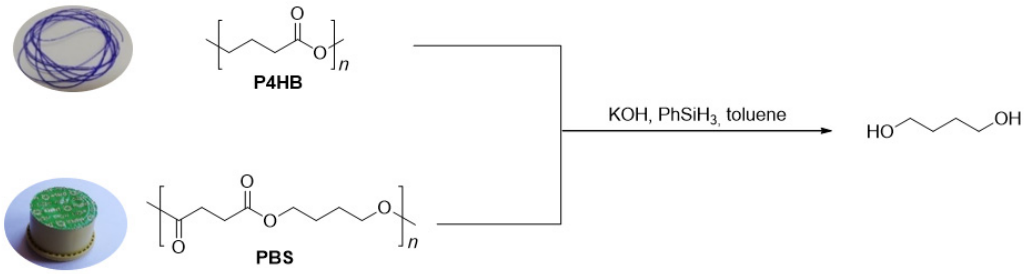
Next, we tested the reductive depolymerization of P4HB and PBS using pinacolborane (HBpin) as the reducing agent catalyzed by $MoO_2Cl_2(H_2O)_2$ (5 mol%). The reaction of P4HB produced $pinBO(CH_2)_4OBpin$ with 71% yield after 24 h in toluene at reflux (Scheme 1). Similarly, the reductive depolymerization of PBS produced $pinBO(CH_2)_4OBpin$ with 73% yield (Scheme 1). During the execution of this work, Cantat and coworkers [44] reported the first methodology for the depolymerization of polyesters using boranes as the reducing agent catalyzed by $La[N(SiMe_3)_2]_3$, but the depolymerization of P4HB and PBS was not investigated in this work. Our methodology has the advantage of using a molybdenum catalyst, which is cheaper and more environmentally friendly than the lanthanum complex.



Scheme 1. Reductive depolymerization of P4HB and PBS waste with the system $MoO_2Cl_2(H_2O)_2$/HBpin.

The development of efficient methodologies for the depolymerization of plastic waste in the absence of a metallic catalyst is also an extremely important issue that needs to be addressed. Nolan and coworkers [45] reported a new procedure for the reduction of esters using the system KOH/$PhSiH_3$, which provides the corresponding alcohols with good yields; however, this catalyst system has never been used in the reductive depolymerization of plastic waste. Based on these results, we decided to apply this methodology to the depolymerization of P4HB and PBS (Table 3).

Table 3. Reductive depolymerization of P4HB and PBS with the system KOH/$PhSiH_3$ [a].



Entry	Polyester	KOH (Equiv.)	Silane	Silane (Equiv.)	Temperature (°C)	Time (h)	Yield (%) [b]
1	P4HB	0.4	$PhSiH_3$	3	110	24	95
2	P4HB	0.4	$PhSiH_3$	2	110	24	38
3	P4HB	0.4	$PhSiH_3$	3	r. t.	24	No reaction
4	P4HB	0.4	TMDS	3	110	24	65
5	P4HB	0.4	PMHS	3	110	48	47
6	PBS	0.8	$PhSiH_3$	6	110	48	61[c]

[a] The reactions were carried out with 0.5 mmol of P4HB, obtained from non-infected surgical suture. [b] Yields were determined by ^{1}H NMR using mesitylene as the internal standard. [c] The reaction was carried out with 0.25 mmol of PBS, obtained from a Delta Q eQo coffee capsule.

The reductive depolymerization of P4HB was performed with KOH (0.4 equiv.) and $PhSiH_3$ (3 equiv.) in toluene at reflux temperature during 24 h, producing 1,4-butanediol with 95% yield (Table 3, entry 1). A similar reaction using only 2 equivalents of $PhSiH_3$ also led to the formation of 1,4-butanediol but with a lower yield of 38% (Table 3, entry 2). In contrast, at room temperature, no product was formed (Table 3, entry 3). When, this reaction was performed with TMDS and PMHS at reflux temperature, 1,4-butanediol was produced with 65% and 47% yields, respectively (Table 3, entries 4 and 5).

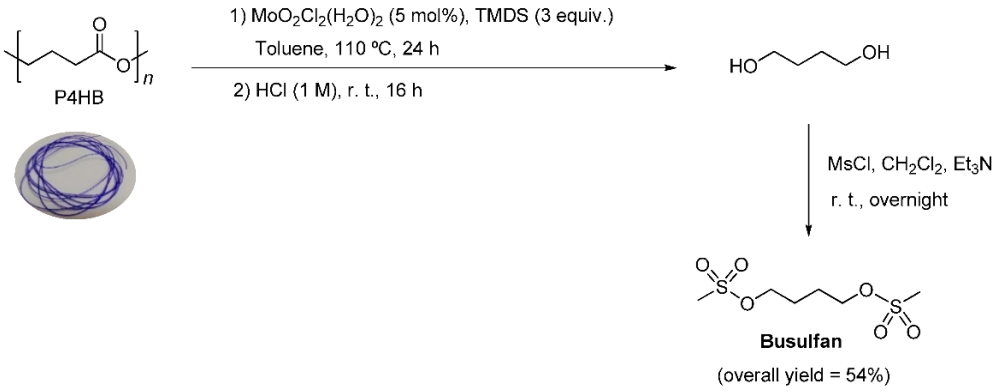
The reductive depolymerization of PBS, obtained from a coffee capsule, was investigated with the catalytic system KOH/ $PhSiH_3$ using 0.8 equivalents of KOH and 6 equivalents of $PhSiH_3$ in toluene at 110 °C for 48 h, leading to the formation of 1,4-butanediol with 61% yield (Table 3, entry 6).

This result demonstrates, for the first time, the applicability of the system KOH/$PhSiH_3$ in the reductive depolymerization of plastic waste. Beyond the excellent yield obtained

from the reductive depolymerization of P4HB, this system also has the advantages of using a cheap base and a non-metallic catalyst.

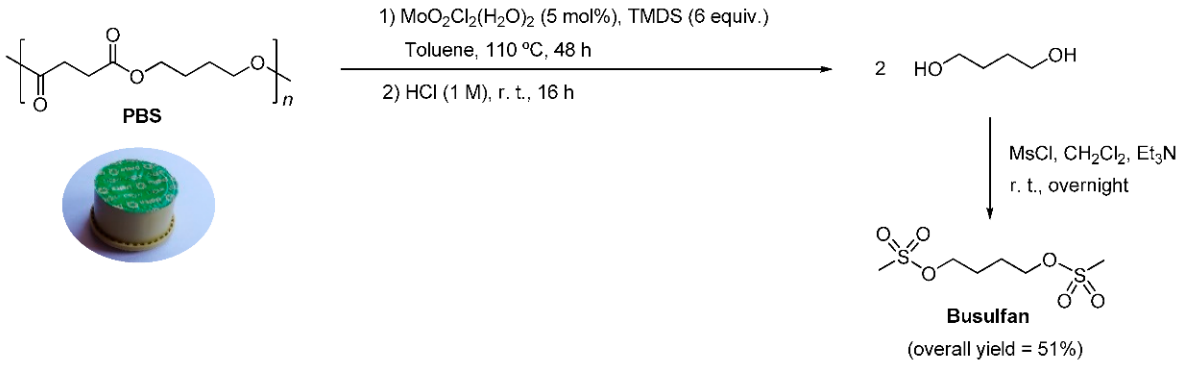
Our next goal was the valorization of 1,4-butanediol, obtained from the depolymerization of P4HB and PBS plastic waste, in the synthesis of compounds of interest to the pharmaceutical industry. Then, we decided to investigate the synthesis of the anticancer drug busulfan from P4HB and PBS plastic waste.

A sample of P4HB, obtained from a non-infected commercial surgical suture, was initially converted to 1,4-butanediol by reductive depolymerization with the catalytic system $MoO_2Cl_2(H_2O)_2$/TMDS, followed by hydrolysis. We decided to use TMDS because this reducing agent has the advantages of being less toxic and expensive. Next, the 1,4-butanediol obtained was mesylated by reaction with methanesulfonyl chloride and triethylamine in dry dichloromethane at room temperature under nitrogen atmosphere, producing busulfan in a moderate overall yield (54%, Figures S3–S5; Scheme 2). This result is very encouraging, suggesting that this method can contribute to a more sustainable production of this drug.



Scheme 2. Synthesis of busulfan from a P4HB surgical suture.

A similar procedure was also developed for the synthesis of busulfan from PBS plastic waste, obtained from a Delta Q eQo coffee capsule, also leading to the formation of 1,4-butanediol, which was then mesylated, giving the anticancer drug busulfan with an overall yield of 51% (Scheme 3).



Scheme 3. Synthesis of busulfan from PBS waste, obtained from a Delta Q eQo coffee capsule.

3. Conclusions

In this work, we reported the first study on the reductive depolymerization of P4HB and PBS plastic waste in moderate to excellent yields. These methodologies involved the use of the catalytic systems $MoO_2Cl_2(H_2O)_2$/TMDS, $MoO_2Cl_2(H_2O)_2$/HBpin and KOH/$PhSiH_3$, which have the advantages of using a cheap and environmentally friendly catalyst or using a non-metallic catalyst. The catalytic systems $MoO_2Cl_2(H_2O)_2$/borane and

$KOH/PhSiH_3$ were applied for the first time in the depolymerization of plastic waste and the results obtained suggest the future application of these systems to the depolymerization of other plastic waste.

We also described the first example of the production of a drug, the anticancer drug busulfan, from plastic waste, namely, P4HB and PBS, with moderate overall yields. This synthetic approach enabled the production of busulfan in a very simple and sustainable way.

The synthesis of busulfan from plastic waste showed a completely new application of plastic waste, adding new options for the circular economy of plastics. New applications could include the use of plastic waste in the total synthesis of other drugs and in the production of pharmaceutical ingredients, allowing the integration of plastic waste into the drug supply chain. However, contaminations or impurities in the raw materials used are a concern and may affect the safety and effectiveness of the drug. Nonetheless, nowadays, the sensitivity of analytical methods to control the quality of the raw materials used in medication, especially in stages near the end, is very high and well regulated.

This work also has other benefits, including the development of new methodologies to recycle and extract value from plastic waste, to reduce the use of fossil resources and to preserve natural sources of carbon. This investigation can also contribute to solving two concerning issues that the planet is currently facing: the impact of plastic pollution and the sustainability of the pharmaceutical industry. Finally, we hope that this work can stimulate both academics and the industry to use plastic waste as a cheap and versatile carbon source.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/catal12040381/s1, Figure S1: 1H NMR spectrum of 1,4-butanediol in CDCl3, Figure S2: 13C NMR spectrum of 1,4-butanediol in CDCl3, Figure S3: 1H NMR spectrum of busulfan in CDCl3, Figure S4: 13C NMR spectrum of busulfan in CDCl3, Figure S5: HPLC-HRMS analysis of a sample of Busulfan. (Ref. [46] cited in the supplementary materials).

Author Contributions: Conceptualization, A.C.F.; methodology, A.C.F.; investigation, D.L.L.; writing—original draft preparation, A.C.F.; writing—review and editing, A.C.F. and D.L.L.; supervision, A.C.F.; All authors have read and agreed to the published version of the manuscript.

Funding: This research was supported by Fundação para a Ciência e Tecnologia (FCT) through projects PTDC/QUI-QOR/0490/2020, (UIDB/00100/2020), UIDP/00100/2020 and LA/P/0056/2020.

Acknowledgments: This research was supported by Fundação para a Ciência e Tecnologia (FCT) through projects PTDC/QUI-QOR/0490/2020, (UIDB/00100/2020), UIDP/00100/2020 and LA/P/0056/2020.

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

References

1. Ellis, L.D.; Rorrer, N.A.; Sullivan, K.P.; Otto, M.; McGeehan, J.E.; Román-Leshkov, Y.; Wierckx, N.; Beskham, G.T. Chemical and Biological Catalysis for Plastics Deconstruction, Recycling, and Upcycling. *Nat. Catal.* **2021**, *4*, 539–556. [CrossRef]
2. Estahbanati, M.R.K.; Kong, X.Y.; Eslami, A.; Soo, H.S. Current Developments in the Chemical Upcycling of Waste Plastics Using Alternative Energy Sources. *ChemSusChem* **2021**, *14*, 4152–4166. [CrossRef]
3. Beghetto, V.; Sole, R.; Buranello, C.; Al-Abkal, M.; Facchin, M. Recent Advancements in Plastic Packaging Recycling: A Mini-Review. *Materials* **2021**, *14*, 4782. [CrossRef]
4. Wang, C.; El-Sepelgy, O. Reductive depolymerization of plastics catalyzed with transition metal complexes. *Curr. Opin. Green Sustain. Chem.* **2021**, *32*, 100547. [CrossRef]
5. Hou, Q.; Zhen, M.; Qian, H.; Nie, Y.; Bai, X.; Xia, T.; Rehman, M.L.U.; Li, Q.; Ju, M. Upcycling and catalytic degradation of plastic wastes. *Cell Rep. Phys. Sci.* **2021**, *2*, 100514. [CrossRef]
6. Kumar, S.; Singh, E.; Mishra, R.; Kumar, A.; Caucci, S. Utilization of Plastic Wastes for Sustainable Environmental Management: A Review. *ChemSusChem* **2021**, *14*, 3985–4006. [CrossRef] [PubMed]
7. Chen, H.; Wan, K.; Zhang, Y.; Wang, Y. Waste to Wealth: Chemical Recycling and Chemical Upcycling of Waste Plastics for a Great Future. *ChemSusChem* **2021**, *14*, 4123–4136. [CrossRef] [PubMed]
8. Qin, Z.-H.; Mou, J.-H.; Chao, C.Y.H.; Chopra, S.S.; Daoud, W.; Leu, S.-Y.; Ning, Z.; Tso, C.Y.; Chan, C.K.; Tang, S.; et al. Biotechnology of Plastic Waste Degradation, Recycling, and Valorization: Current Advances and Future Perspectives. *ChemSusChem* **2021**, *14*, 4103–4114. [CrossRef] [PubMed]

9. Jönsson, C.; Wei, R.; Biundo, A.; Landberg, J.; Bour, L.S.; Pezzotti, F.; Toca, A.; Jacques, L.M.; Bornscheuer, U.T.; Syrén, P.-O. Biocatalysis in the Recycling Landscape for Synthetic Polymers and Plastics towards Circular Textiles. *ChemSusChem* **2021**, *14*, 4028–4040. [CrossRef] [PubMed]
10. Miao, Y.; Jouanne, A.v.; Yokochi, A. Current Technologies in Depolymerization Process and the Road Ahead. *Polymers* **2021**, *13*, 449. [CrossRef]
11. McKeown, P.; Jones, M.D. The Chemical Recycling of PLA: A Review. *Sus. Chem.* **2020**, *1*, 1–22. [CrossRef]
12. Jiang, J.; Shi, K.; Zhang, X.; Yu, K.; Zhang, H.; He, J.; Ju, Y.; Liu, J. From plastic waste to wealth using chemical recycling: A Review. *J. Environ. Chem. Eng.* **2020**, *10*, 106867. [CrossRef]
13. Sardon, H.; Dove, A.P. Organocatalysis for depolymerization. *Polym. Chem.* **2019**, *10*, 172–186.
14. Tang, X.; Chen, E.Y.-X. Toward Infinitely Recyclable Plastics Derived from Renewable Cyclic Esters. *Chem* **2019**, *5*, 284–312. [CrossRef]
15. Hong, M.; Chen, E.Y.-X. Chemically Recyclable Polymers: A Circular Economy Approach to Sustainability. *Green Chem.* **2017**, *19*, 3692–3706. [CrossRef]
16. Fernandes, A.C. Reductive Depolymerization as an Efficient Methodology for the Conversion of Plastic Waste into Value-added Compounds. *Green Chem.* **2021**, *23*, 7330–7360. [CrossRef]
17. Krall, E.M.; Klein, T.W.; Andersen, R.J.; Nett, A.J.; Glasgow, R.W.; Reader, D.S.; Dauphinais, B.C.; Mc Ilrath, S.P.; Fischer, A.A.; Carney, M.J.; et al. Controlled Hydrogenative Depolymerization of Polyesters and Polycarbonates Catalyzed by Ruthenium(II) PNN Pincer Complexes. *Chem. Commun.* **2014**, *50*, 4884–4887. [CrossRef] [PubMed]
18. Fuentes, J.A.; Smith, S.M.; Scharbert, M.T.; Carpenter, I.; Cordes, D.B.; Slawin, A.M.Z.; Clarke, M.L. On the Functional Group Tolerance of Ester Hydrogenation and Polyester Depolymerisation Catalysed by Ruthenium Complexes of Tridentate Aminophosphine Ligands. *Chem. Eur. J.* **2015**, *21*, 10851–10860. [CrossRef]
19. Westhues, S.; Idel, J.; Klankermayer, J. Molecular catalyst systems as key enablers for tailored polyesters and polycarbonate recycling concepts. *Sci. Adv.* **2018**, *4*, eaat9669. [CrossRef] [PubMed]
20. Feghali, E.; Cantat, T. Room Temperature Organocatalyzed Reductive Depolymerization of Waste Polyethers, Polyesters, and Polycarbonates. *ChemSusChem* **2015**, *8*, 980–984. [CrossRef] [PubMed]
21. Monsigny, L.; Berthet, J.-C.; Cantat, T. Depolymerization of Waste Plastics to Monomers and Chemicals Using a Hydrosilylation Strategy Facilitated by Brookhart's Iridium(III) Catalyst. *ACS Sustain. Chem. Eng.* **2018**, *6*, 10481–10488. [CrossRef]
22. Shao, Z.; Zhong, R.; Ferraccioli, R.; Li, Y.; Liu, Q. General and Phosphine-Free Cobalt-Catalyzed Hydrogenation of Esters to Alcohols. *Chin. J. Chem.* **2019**, *37*, 1125–1130. [CrossRef]
23. Farrar-Tobar, R.A.; Wozniak, B.; Savini, A.; Hinze, S.; Tin, S.; de Vries, J.G. Base-Free Iron Catalyzed Transfer Hydrogenation of Esters Using EtOH as Hydrogen Source. *Angew. Chem. Int. Ed.* **2019**, *58*, 1129–1133. [CrossRef] [PubMed]
24. Nunes, B.F.S.; Oliveira, M.C.; Fernandes, A.C. Dioxomolybdenum Complex as an Efficient and Cheap Catalyst for the Reductive Depolymerization of Plastic Waste into Value-added Compounds and Fuels. *Green Chem.* **2020**, *22*, 2419–2425. [CrossRef]
25. Fernandes, A.C. Reductive Depolymerization of Plastic Waste Catalyzed by Zn(OAc)2·2H2O. *ChemSusChem* **2021**, *14*, 4228–4233. [CrossRef] [PubMed]
26. Fernandes, A.C. Recent Advances in the Synthesis of Nitrogen Compounds from Biomass Derivatives. In *Methodologies in Amine Synthesis. Challenges and Applications*; Wiley-VCH: Weinheim, Germany, 2020; pp. 341–376.
27. Elangovan, S.; Afanasenko, A.; Haupenthal, J.; Sun, Z.; Liu, Y.; Hirsch, A.K.H.; Barta, K. From Wood to Tetrahydro-2-benzazepines in Three Waste-Free Steps: Modular Synthesis of Biologically Active Lignin-Derived Scaffolds. *ACS Cent. Sci.* **2019**, *5*, 1707–1716. [CrossRef] [PubMed]
28. Caetano, J.A.T.; Fernandes, A.C. One-pot Synthesis of Amines from Biomass Resources Catalyzed by HReO4. *Green Chem.* **2018**, *20*, 2494–2498. [CrossRef]
29. Isca, V.M.S.; Fernandes, A.C. Direct Synthesis of α-Aminophosphonates from Biomass Resources Catalyzed by HReO4. *Green Chem.* **2018**, *20*, 3242–3245. [CrossRef]
30. Jia, L.L.; Zhang, Z.; Qiao, Y.; Pedersen, C.M.; Ge, H.; Wei, Z.; Deng, T.; Ren, J.; Liu, X.; Wang, Y.; et al. Product Distribution Control for Glucosamine Condensation: Nuclear Magnetic Resonance (NMR) Investigation Substantiated by Density Functional Calculations. *Ind. Eng. Chem. Res.* **2017**, *56*, 2925–2934. [CrossRef]
31. Song, L.; Zheng, M.; Pang, J.; Sebastian, J.; Wang, W.; Qu, M.; Zhao, J.; Wang, X.; Zhang, T. One-pot Synthesis of 2-Hydroxymethyl-5-methylpyrazine from Renewable 1,3-Dihydroxyacetone. *Green Chem.* **2017**, *19*, 3515–3519. [CrossRef]
32. Chen, X.; Chew, S.L.; Kerton, F.M.; Yan, N. Direct Conversion of Chitin into a N-containing Furan Derivative. *Green Chem.* **2014**, *16*, 2204–2212. [CrossRef]
33. Buggia, I.; Locatelli, F.; Regazzi, M.B.; Zecca, M. Busulfan. *Ann. Pharm.* **1994**, *28*, 1055–1062. [CrossRef] [PubMed]
34. Iwamoto, T.; Hiraku, Y.; Oikawa, S.; Mizutani, H.; Kojima, M.; Kawanishi, S. DNA Intrastrand Cross-link at the 5′-GA-3′ Sequence Formed by Busulfan and its Role in the Cytotoxic Effect. *Cancer Sci.* **2004**, *95*, 454–458. [CrossRef]
35. Krivoy, N.; Hoffer, E.; Lurie, Y.; Bentur, Y.; Rowe, M. Busulfan Use in Hematopoietic Stem Cell Transplantation: Pharmacology, Dose Adjustment, Safety and Efficacy in Adults and Children. *Curr. Drug Saf.* **2008**, *3*, 60–66. [CrossRef] [PubMed]
36. Myers, A.L.; Kawedia, J.D.; Champlin, R.E.; Kramer, M.A.; Nieto, Y.; Ghose, R.; Andersson, B.S. Clarifying Busulfan Metabolism and Drug Interactions to Support New Therapeutic Drug Monitoring Strategies: A Comprehensive Review. *Expert Opin. Drug Metab. Toxicol.* **2017**, *13*, 901–923. [CrossRef] [PubMed]

37. Shiri, P.; Ramezanpour, S.; Amani, A.M.; Dehaen, W. A patent review on efficient strategies for the total synthesis of pazopanib, regorafenib and lenvatinib as novel anti-angiogenesis receptor tyrosine kinase inhibitors for cancer therapy. *Mol. Divers.* **2022**, 1–22. [CrossRef]
38. Wang, L.; Li, R.; Song, C.; Chen, Y.; Long, H.; Yang, L. Small-Molecule Anti-Cancer Drugs From 2016 to 2020: Synthesis and Clinical Application. *Nat. Prod. Commun.* **2021**, *16*, 1–42. [CrossRef]
39. Noronha, R.G.; Fernandes, A.C. High Valent Oxo-Molybdenum Complexes as Efficient Catalysts for C-X Bond Forming Reactions. *Curr. Org. Chem.* **2012**, *16*, 33–64. [CrossRef]
40. Pereira, J.G.; Sousa, S.C.A.; Fernandes, A.C. Direct Conversion of Carbohydrates into 5-Ethoxymethylfurfural (EMF) and 5-Hydroxymethylfurfural (HMF) Catalyzed by Oxomolybdenum Complexes. *ChemistrySelect* **2017**, *2*, 4516–4521. [CrossRef]
41. Sousa, S.C.A.; Fernandes, T.A.; Fernandes, A.C. Highly Efficient Deoxygenation of Aryl Ketones to Arylalkanes Catalyzed by Dioxidomolybdenum Complexes. *Eur. J. Org. Chem.* **2016**, *2016*, 3109–3112. [CrossRef]
42. Fernandes, T.A.; Fernandes, A.C. Dioxomolybdenum Complexes as Excellent Catalysts for the Deoxygenation of Aryl Ketones to Aryl Alkenes. *ChemCatChem* **2015**, *7*, 3503–3507. [CrossRef]
43. Sousa, S.C.A.; Bernardo, J.R.; Wolff, M.; Machura, B.; Fernandes, A.C. Oxo-Rhenium(V) Complexes Containing Heterocycling Ligands as Catalysts for the Reduction of Sulfoxides. *Eur. J. Org. Chem.* **2014**, *2014*, 1855–1859. [CrossRef]
44. Kobylarski, M.; Berthet, J.-C.; Cantat, T. Reductive Depolymerization of Polyesters and Polycarbonates with Hydroboranes by Using a Lanthanum($_{III}$) tris(amide) Catalyst. *Chem. Commun.* **2022**, *58*, 2830–2833. [CrossRef] [PubMed]
45. Fernández-Salas, J.A.; Manzini, S.; Nolan, S.P. Facile and efficient KOH-Catalysed Reduction of Esters and Tertiary Amides. *Chem. Commun.* **2013**, *49*, 9758–9760. [CrossRef] [PubMed]
46. Arnáiz, F.J.; Aguado, R.; Pedrosa, M.R.; De Cian, A. Addition compounds of dichlorodioxomolybdenum(VI) with sulfoxides. Molecular structure of $[MoO_2Cl_2(Me_2SO)_2]$. *Inorg. Chim. Acta* **2003**, *347*, 33. [CrossRef]