Manganese Catalysed Dehydrogenative Synthesis of Polyureas from Diformamide and Diamines

Angus McLuskie,[a] Claire N Brodie,[a] Michele Tricarico,[b] Chang Gao,[a] Gavin Peters,[a] C. Logan Mackay,[c] Jin-Chong Tan,*[b] Amit Kumar[a]*

a School of Chemistry, University of St. Andrews, North Haugh, St. Andrews, KY169ST, UK. Email: ak336@st-andrews.ac.uk
b Department of Engineering Science, University of Oxford, Parks road, Oxford. OX13PJ, UK. Email: jin-chong.tan@eng.ox.ac.uk
c School of Chemistry, University of Edinburgh, EH93FJ.

We report here the synthesis of polyureas from the dehydrogenative coupling of diamines and diformamides. The reaction is catalysed by a manganese pincer complex and releases H_2 gas as the only by-product making the process atom-economic and sustainable. This work advances the current state-of-the-art by replacing a toxic feedstock – diisocyanates (used to make polyureas) with a safer feedstock – diformamides and using a catalyst based on an earth-abundant metal. We also report here the physical and mechanical properties of the isolated polyureas. We suggest that the reaction proceeds via isocyanate intermediates that are formed by the manganese catalysed dehydrogenation of formamides.

Polyureas are useful plastics with applications in the construction, coating, and biomedical industries.[1–3] Their global market is £780 million per year and is expected to grow to £1.4 billion by 2030.[4] Polyureas are industrially made from the reaction of diamines with diisocyanates; diisocyanates are made from phosgene gas. Both disocyanates and phosgene gas are extremely toxic and hazardous to human health and the environment. Thus, there is an urgent need to develop greener methods that avoid toxic reagents for the synthesis of polyureas. .[15–17] However, they suffer from the issues of limited substrate scope, low selectivity, or the use of harsh reaction conditions or specialty solvents.

Catalytic dehydrogenation is a green and atom-economic approach to the synthesis of organic compounds.[18–20] The synthesis of urea derivatives has been reported from the dehydrogenative coupling of amines and methanol using ruthenium and iron pincer catalysts by Hong[21] and Bernskoetter,[22] respectively. Milstein has reported the synthesis of urea derivatives by the dehydrogenative coupling of formamide with amines in the presence of a ruthenium pincer catalyst.[23] Gunanathan has reported the synthesis of urea derivatives from the coupling of N,N'-dimethylformamide, and amine where dimethylamine was observed as a by-product.[24]

A few methods that avoid diisocyanates have been reported for the synthesis of polyureas. For example, polyureas can be made from the condensation of diamines with CO_2, however, either a dehydrating agent or a high temperature (>150 °C) is needed for this process.[5–11]The use of other carbonylating agent such as urea,[12] carbamate[13], or biscarbamate[14] instead of diisocyanates have also been demonstrated for the synthesis of polyureas.

We have recently expanded the concept of the dehydrogenative synthesis of urea derivatives and reported a new method for the synthesis of polyureas from the dehydrogenative coupling of diamines and methanol using ruthenium[25] and manganese pincer complexes.[26] Liu has also reported the synthesis of polyureas from the dehydrogenative coupling of diamines and methanol using analogous manganese pincer complexes.[27] The discovered method substitutes diisocyanates with methanol which is relatively much less toxic. Additionally, methanol is cheaper and renewable which makes the process potentially more sustainable.[28] However, this method has two limitations:

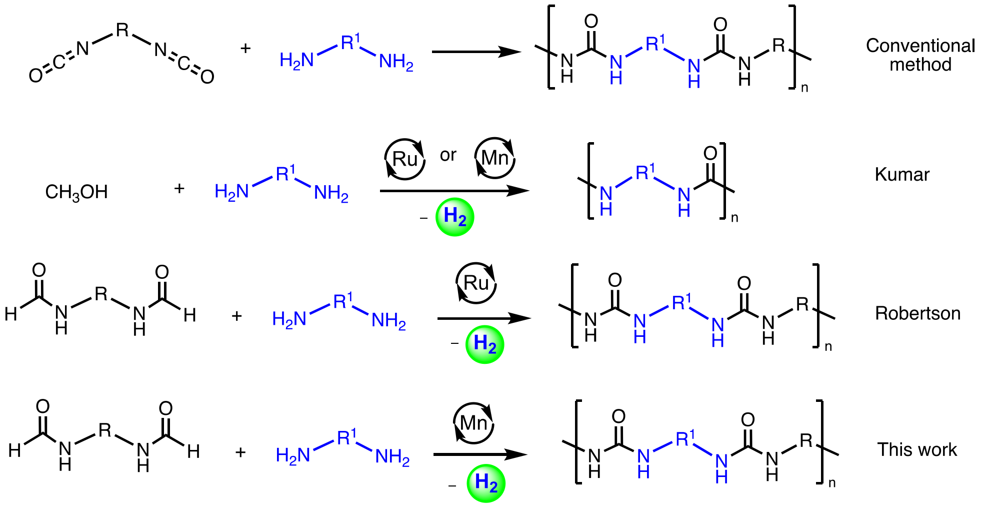
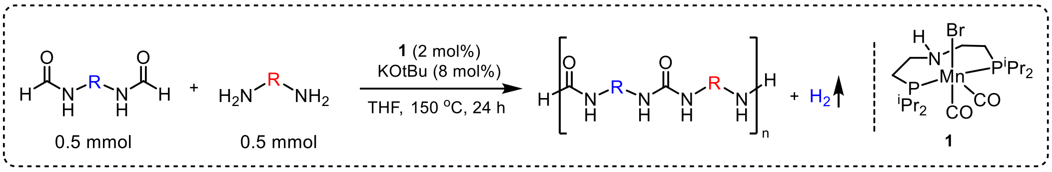
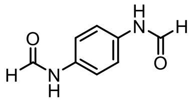
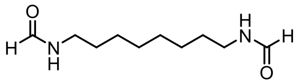


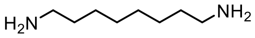
Figure 1. Synthesis of polyureas using conventional and dehydrogenative routes.

Table 1. Catalytic conditions for the synthesis of polyureas from diformamides and diamines.




DF1


DF2


DA1

Entry	Diformamide	Diamine	Base	Solvent	N_2	Yield	M_n (MALDI)	Al:Ar	T_d (°C)	T_m (°C)
1	DF1	DA1	KO^{t}Bu	THF	Sealed	82%	1877	1.67	246	221
2	DF1	DA1	KO^{t}Bu	Anisole	Sealed	77%	2111	1.03	246	220
3	DF1	DA1	KO^{t}Bu	Anisole	Open	32%	2111	1.67	237	201
4	DF1	DA1	KO^{t}Bu	Diglyme	Open	79%	1904	2.01	238	212
5	DF1	DA1	KO^{t}Bu	DMSO	Open	44%	A/W	4.88	266	211
6	DF1	DA1	K_2CO_3	Anisole	Open	30%	1770	1.73	242	204
7	DF2	DA1	KO^{t}Bu	Anisole	Open	85%	2111	N/A	-	-
8	DF2	DA1	KO^{t}Bu	Diglyme	Open	25%	2110	N/A	-	-
9	DF2	DA1	KO^{t}Bu	THF	Open	78%	2594	N/A	247	215

[a]Catalytic conditions: Diamine (0.5 mmol), diamine (0.5 mmol), solvent (2 mL), Complex **1** (2 mol%), and KO^{t}Bu (8 mol%). Reactions were carried out in 250 mL Young's flasks. Al:Ar = Aliphatic:Aromatic NMR integral relationship (see example in ESI). M_n (MALDI): value is estimated as the maximum signal observed in MALDI-FT-ICR MS. T_d (Decomposition temperature°C) was recorded at 5% mass loss. T_m stands for melting temperature.

(a) **Molecular weight issue**: The need for high temperature (150 °C) makes it difficult to use methanol under open conditions due to its low boiling point (64.7 °C) because of which reactions were conducted in the sealed system. This limits the polymer chain length or their molecular weight due to the accumulation of H_2 gas in the system which can disfavour the dehydrogenation reaction. (b) **Functionality issue**: Only one type of functionality (e.g. aliphatic/aromatic) could be incorporated in the polyurea using this method whereas the conventional methodology can make polyurea containing two different functionality – one coming from diisocyanate and the other one from diamine. This is particularly useful for various applications where a rigid/hard segment (from an aromatic group) and a flexible segment (from alkyl chains) are needed in the polymer. The presence of hard and soft segments in polyureas leads to a unique microphase separation in the polymer microstructure that leads to excellent macroscopic properties, such as stability, high strength, and aging resistance.[29]

An alternative approach to overcome these limitations is to make polyureas from the dehydrogenative coupling of diformamides and diamines. This approach has been recently demonstrated by Robertson using a ruthenium pincer catalyst.[30] However, the use of precious metals such as ruthenium raises concerns of sustainability due to their high cost and low abundance on the earth's crust. The use of a catalyst based on an earth-abundant metal such as manganese which is the third most abundant transition-metal on earth's crust can make the process more cost-effective and sustainable. We report here that a manganese pincer complex **1** can catalyse the dehydrogenative coupling of diformamides and diamines to form polyureas. We also present their chemical (spectroscopy, mass spectrometry), physical (melting, decomposition, crystallization, and glass-transition temperatures), and mechanical (indentation modulus, hardness) properties of the synthesized polyureas.

We started our investigation by studying the reaction of N,N'-(1,4-phenylene)diformamide (**DF1**, 0.5 mmol) with diaminooctane (**DA1**, 0.5 mmol) in the presence of a manganese pincer complex (**1**, 1 mol%) and KO^{t}Bu (4 mol%) in a sealed system. Performing the reaction at 150 °C, in THF under sealed conditions for 24 h led to the isolation of an off-white solid in 82% yield (Table1, entry 1). The product did not dissolve in common solvents such as water, THF, toluene, DCM, and $CHCl_3$. It exhibited partial solubility in TFA (trifluoroacetic acid) that was used for the NMR analysis. ^1H and ^{13}C NMR spectra showed signals corresponding to both aliphatic and aromatic protons that would come from (aliphatic) diamines and (aromatic) diformamides. The end group analysis of the partially soluble sample showed the molecular weight to be 1657 Da at the end of the 24 h reaction period. In the case of Robertson's report on the ruthenium catalysed synthesis of polyureas from diformamides and diamines, the molecular weight (M_n) of a polyurea was found to significantly increase after 1 day of reaction time (e.g. 3700 Da after day 1, 13,300 Da after day 2, and 32,800 Da after day 3) in a manner expected for a step growth polymerisation mechanism.[28] However, in our case, the formation of insoluble/poorly soluble material at the end of the polymerisation reaction has made the estimation of molecular weight difficult.

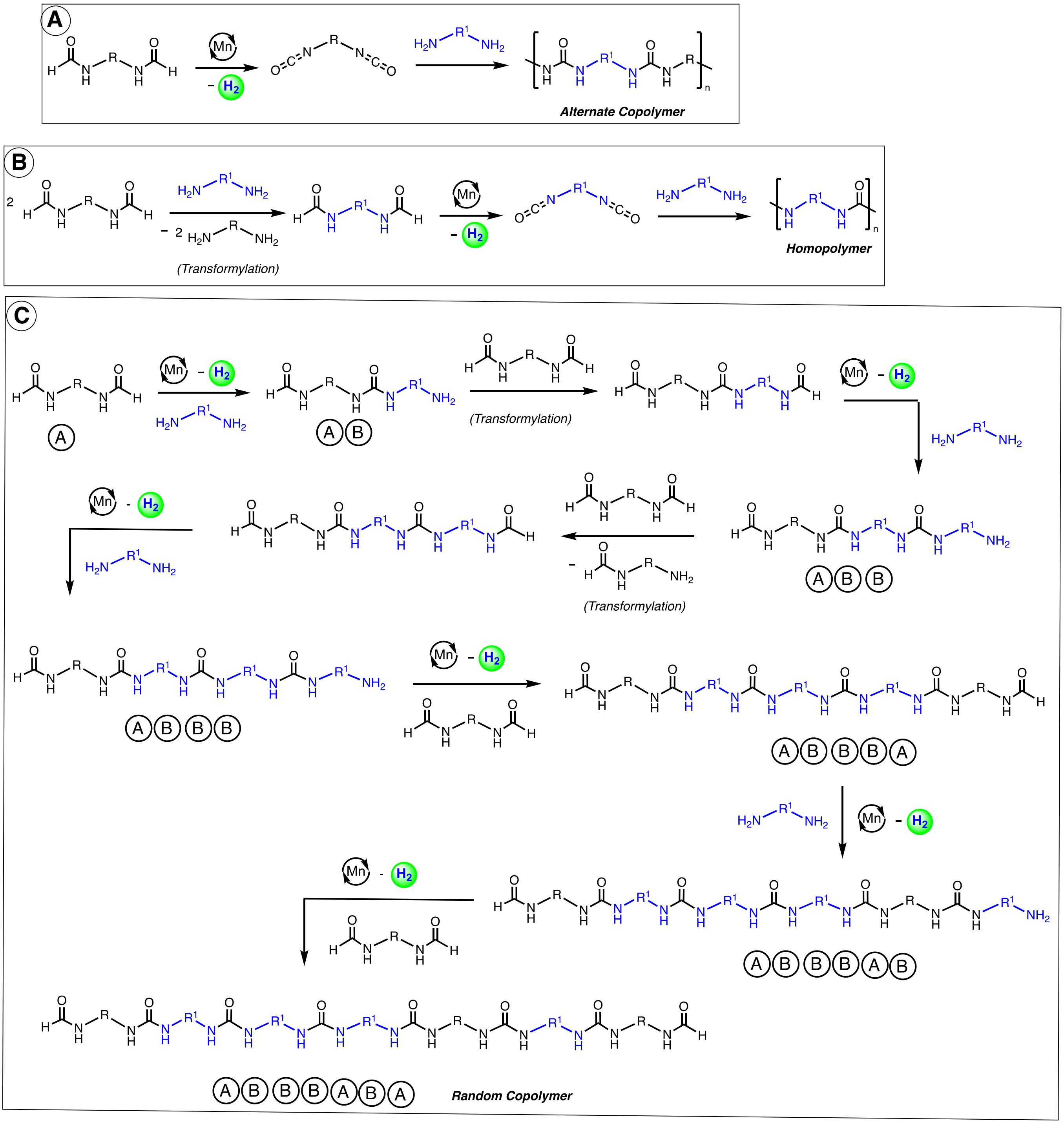


Figure 2. Proposed pathway for the formation of alternate copolymer, homopolymer and random copolymer from the manganese catalysed dehydrogenative coupling of diformamides and diamines.

The insolubility of polyureas from the reaction of diformamides and diamines such as diaminooctane and m-xylenediamine were also observed by Robertson and therefore Jeffamine® was used in combination with diamines and diformamides to make soluble polyureas.[30] The IR spectrum of the polyurea (entry 1) showed a signal at 1680 cm^{-1} corresponding to the carbonyl stretching frequency and at 1576 cm^{-1} corresponding to N-H bending both characteristic of a urea functional group. Interesting insights were obtained from the MALDI-FT-ICR mass spectrometry studies that showed the presence of repeating units corresponding to copolymers formed from aromatic diformamide (**DF1**) and aliphatic diamine (**DA1**). Mass spectrometry data showed that polymers contained all combinations of end groups: amine, amine; formyl, formyl; and formyl, amine. More interestingly, the mass spectrometry (MALDI-FT-ICR MS) data revealed that the formed material is a mixture of copolymer (formed from **DF1**+**DA1**) as well as homopolymer (resulting only from **DA1**). We speculate that the formation of the latter occurs via the transformylation of **DA1** with **DF1** with the elimination of p-phenylenediamine (Figure 2). Such transformylation reaction has been reported by us and others in the past.[26] Considering the insoluble nature of the isolated material it is not possible to determine the exact ratio of homopolymer and copolymer. However, for an approximate comparison in different reaction conditions, we have provided the ratio of the integration of aliphatic vs aromatic signals from the ^{1}H NMR spectra. These need to be used with caution as the isolated materials are not completely soluble in d-TFA. TGA (thermogravimetric analysis) and DSC (differential scanning calorimetry) studies were conducted to estimate the decomposition temperature (T_d) and melting temperature (T_m) of the polyurea which was found to be 246°C and 221°C respectively in this case.

Changing the solvent to anisole keeping the remaining conditions the same led to the observation of similar composition of polymers, albeit at a slightly reduced yield (77%, Table1, entry 2) with respect to that in the case of THF (entry 1). Interestingly, when the solvent is changed to diglyme and the catalysis is carried out in open conditions under the flow of N_2 (entry 4), the MALDI-FT-ICR mass spectrometry showed a higher abundance of signals corresponding to co-polymers than those to homopolymers from the transformylation reaction (see SI). The product was isolated in 79% yield. However, when the solvent was switched to DMSO (entry 5), a significant reduction in yield (44%) was obtained. An experiment carried out in anisole with a change in base to K_2CO_3 led to a low yield of 30%.

We next expanded our substrate scope by changing the diformamide to **DF2** (N,N'-(octane-1,8-diyl)diformamide). The "R" groups of **DF2** and **DA1** are identical, so, regardless of transformylation, a reaction of these together would generate polymers of the same chemical structure, and identical to the polyurea made from the dehydrogenative coupling of 1,8-diaminooctane and methanol as previously reported by us using a manganese pincer complex **1**. The catalytic studies were conducted in anisole, diglyme, THF, and DMSO under the open flow of nitrogen. Anisole and THF led to higher yields (84% and 78%) whereas lower yields were obtained in the case of diglyme and DMSO as described in table 2. T_d (242 °C) and T_m (204 °C) in the case of polyurea made from **DF2** and **DA1** were found to be higher than that of polyurea made from **DA1** and methanol (T_d, 190 °C and Tm:) under the same reaction condition: complex **1** (1 mol%), KO^{t}Bu (4 mol%), 150 °C, 24 h THF. Since the best yield for the reaction of **DF2** and **DA1** was obtained in anisole under open conditions, we expanded the substrate scope for the polyurea synthesis by conducting reactions of **DF1** and **DF2** with 3,3'-methylenebis(cyclohexan-1-amine) (**DA2**) and p-xylenediamine (**DA3**) in anisolen under an open flow of nitrogen. However, relatively lower yields of polyureas were obtained in these cases as described in Table 1.

To get an understanding of the mechanical properties of polyureas made from this method, we performed nanoindentation analysis of polyureas made from **DF1** and **DA1** (Table 1, entry 4) as well as from **DF2** and **DA2** (Table 1, entry 7). The tests were carried out using a KLA iMicro nanoindenter, equipped with a 50mN force actuator and a Berkovich tip. Continuous Stiffness Measurements (CSM) were performed, allowing to measure the indentation modulus E* ($E^* = E/1-\nu^2$) which can be used in place of Young's modulus E when the Poisson's ratio ν is unknown. Our studies showed a high indentation modulus of 4.25±0.72 GPa and a hardness of 252±64 MPa for polyurea made from N,N'-(1,4-phenylene)diformamide (**DF1**) and diaminooctane (**DA1,** entry 4) and indentation modulus of 4.93±0.63 GPa and a hardness of 291±59 MPa for the polyurea made using aliphatic diformamide (**DF2**) and diaminooctane (**DA2**, entry 7). The Elastic modulus of a commercial polyurea XS-350 has been reported to be less than what we observe here (100 MPa).[31]

In our recent work on the manganese catalysed synthesis of urea derivatives from formamides and amines, we reported a mechanism supported by the DFT computation where the manganese complex **2** dehydrogenates a formamide to form an isocyanate followed by its subsequent reaction with an amine to form a urea derivative.[26] We speculate that the synthesis of polyureas from diformamides and diamines proceeds via a similar pathway. To probe further, we monitored the reaction at a stoichiometric and catalytic level using NMR spectroscopy. The reaction of complex **1** with KO^{t}Bu (1.2 equivalents) in an NMR tube in toluene-d8 immediately resulted in the formation of the amido-complex **2** as also previously reported.[30] Interestingly, the addition of 2 equivalents of formamide ($HCONH_2$) to the in-situ formed complex **2** formed a new complex as evidenced by the complete consumption of the signal corresponding to **2** (δ 113.0) and the appearance of a new signal in the $^{31}P\{^1H\}$ NMR spectrum (δ 87.2). Analysis of the ^1H and $^{13}C\{^1H\}$ NMR spectra suggest the formation of complex **3** through N-H activation of formamide via metal-ligand cooperation. Interestingly, heating the NMR tube containing complex **3** at 110 °C for 4 days led to a clean formation of a new complex ($^{31}P\{^1H\}$ NMR: δ 88.6) characterised as the manganese-isocyanate complex **4**. These results are in agreement with a recent report by Milstein where a ruthenium-PNP complex was found to activate and dehydrogenate formamide to form a ruthenium-coordinated isocyanate complex.[23] We observed similar reactivities when complex **2** was reacted with N-methyl formamide and formanilide. The N-H activation of N-methyl formamide and formanilide by complex **2** has been previously reported by Boncella and Tondreau and our spectral data are in agreement with those reported.[32] Interestingly, conducting a GC-MS analysis of the reaction mixture obtained after heating complex **2** with 2 equivalents of formanilide (4 days) in an NMR tube (as described above) showed the presence of phenyl isocyanate. The formation of complexes **3** and **4** was also obtained in catalyst speciation studies when we measured the NMR spectra for samples taken after 0h, 2h, 6h and 24 h from the catalytic experiment as described in Table 1, entry 1. These observations support our hypothesis that the manganese complex **3** is capable of dehydrogenating formamide and forming an isocyanate intermediate that can further react with an amine to form a urea functional group.

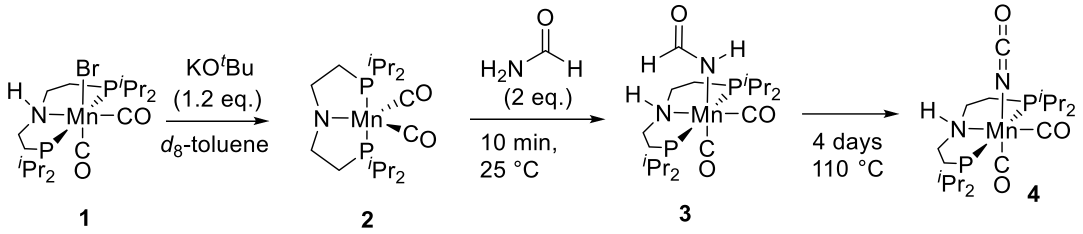


Figure 3. Reaction of formamide with *in-situ* generated complex **2**.

In conclusion, we report here the synthesis of polyureas from the manganese-catalysed dehydrogenative coupling of diformamides with diamines. Polyureas have been characterized by NMR and IR spectra as well as MALDI-FT-ICR mass spectrometry that shows that under these conditions random copolymers facilitated by transformylation reactions are formed (Figure 2). Based on our experimental studies and previous report by us, we propose that the reaction proceeds by the dehydrogenation of diformamides to form diisocyanates followed by its reaction with diamines to form polyureas. The current methodology replaces the use of toxic diisocyanates with a safer feedstock – diformamides. The use of an earth-abundant metal-based catalyst is an added advantage that makes the process more sustainable.

References

[1] B. Shojaei, M. Najafi, A. Yazdanbakhsh, M. Abtahi, C. Zhang, *Polym Adv Technol* **2021**, *32*, 2797–2812.

[2] P. Rocas, C. Cusco, J. Rocas, F. Albericio, *Curr Drug Deliv* **2018**, *15*, DOI 10.2174/1567201814666171019102537.

[3] M. Tripathi, S. Parthasarathy, P. K. Roy, *J Appl Polym Sci* **2020**, *137*, DOI 10.1002/app.48573.

[4] "Polyurea Coatings Market Global Forecast to 2025 | MarketsandMarkets," can be found under https://www.marketsandmarkets.com/Market-Reports/polyurea-coatings-market-152676861.html?gclid=Cj0KCQjw8rT8BRCbARIsALWiOvRwzrAtBwMcCRV3eXvOYKIdHfFk5OpjWw5rp5oVMIpe50yRVEX5LHcaAkN0EALw_wcB, **n.d.**

[5] P. Wang, Y. Fei, Y. Long, Y. Deng, *Journal of CO2 Utilization* **2018**, *28*, 403–407.

[6] S. Jiang, H. Y. Cheng, R. H. Shi, P. X. Wu, W. W. Lin, C. Zhang, M. Arai, F. Y. Zhao, *ACS Appl Mater Interfaces* **2019**, *11*, 47413–47421.

[7] S. Jiang, R. Shi, H. Cheng, C. Zhang, F. Zhao, *Green Energy and Environment* **2017**, *2*, 370–376.

[8] P. Wang, X. Ma, Q. Li, B. Yang, J. Shang, Y. Deng, *RSC Adv* **2016**, *6*, 54013–54019.

[9] P. Wang, Y. Fei, Y. Deng, *New Journal of Chemistry* **2018**, *42*, 1202–1207.

[10] J. Shang, S. Liu, X. Ma, L. Lu, Y. Deng, *Green Chemistry* **2012**, *14*, 2899–2906.

[11] T. Jiang, X. Ma, Y. Zhou, S. Liang, J. Zhang, B. Han, *Green Chemistry* **2008**, *10*, 465–46.

[12] J. M. Sirrine, S. A. Schexnayder, J. M. Dennis, T. E. Long, *Polymer (Guildf)* **2018**, *154*, 225–232.

[13] N. Kébir, M. Benoit, C. Legrand, F. Burel, *Eur Polym J* **2017**, *96*, 87–96.

[14] H. Y. Chen, W. C. Pan, C. H. Lin, C. Y. Huang, S. A. Dai, *Journal of Polymer Research* **2012**, *19*, DOI 10.1007/s10965-011-9754-8.

[15] F. Bigi, R. Maggi, G. Sartori, *Green Chemistry* **2000**, *2*, 140–148.

[16] T. P. Vishnyakova, I. A. Golubeva, E. v Glebova, *Russian Chemical Reviews* **1985**, *54*, 249–261.

[17] M. Soccio, R. Mazzoni, C. Lucarelli, S. Quattrosoldi, A. Cingolani, M. Fiorini, N. Lotti, T. Tabanelli, *ACS Sustain Chem Eng* **2020**, DOI 10.1021/acssuschemeng.0c05177.

[18] A. Kumar, C. Gao, *ChemCatChem* **2021**, *13*, 1105–1134.

[19] A. Kumar, P. Daw, D. Milstein, *Chem Rev* **2022**, *122*, 385–441.

[20] C. Gunanathan, D. Milstein, *Science (1979)* **2013**, *341*, 257–261.

[21] S. H. Kim, S. H. Hong, *Org Lett* **2016**, *18*, 212–215.

[22] E. M. Lane, N. Hazari, W. H. Bernskoetter, *Chem Sci* **2018**, *9*, 4003–4008.

[23] J. Bruffaerts, N. von Wolff, Y. Diskin-Posner, Y. Ben-David, D. Milstein, *J Am Chem Soc* **2019**, *141*, 16486–16493.

[24] V. Krishnakumar, B. Chatterjee, C. Gunanathan, *Inorg Chem* **2017**, *56*, 7278–7284.

[25] A. Kumar, D. Armstrong, G. Peters, M. Nagala, S. Shirran, *Chemical Communications* **2021**, DOI 10.1039/D1CC01121A.

[26] A. E. Owen, A. Preiss, A. McLuskie, C. Gao, G. Peters, M. Bühl, A. Kumar, *ACS Catal* **2022**, *12*, 6923–6933.

[27] J. Guo , J. Tang , H. Xi , S.-Y. Zhao , W. Liu , Man-Chinese Chemical Letters (2022), doi: https://doi.org/10.1016/j.cclet.2022.08.01

[28] Q. I. Roode-Gutzmer, D. Kaiser, M. Bertau, *ChemBioEng Reviews* **2019**, *6*, 209–236.

[28] C. R. Langsted, S. W., Paulson, and co-workers, *J. Appl. Polym. Sci.* **2022**, 139, e52088.

[29] T. Choi, D. Fragiadakis, C. M. Roland and J. Runt, *Macromolecules*, 2012, **45**, 3581–3589.

[30] H. Wang, W. Deng, H. Wu, A. Pi, J. Li and F. Huang, *Def. Technol.*, 2019, **15**, 875-884.

[31] D. H. Nguyen , X. Trivelli , F. Capet , J.-F. Paul , F. Dumeignil and R. M. Gauvin, *ACS Catal.*, 2017, **7** , 2022-2032.

[32] N. H. Anderson , J. M. Boncella and A. M. Tondreau , *Organometallics*, 2018, **37** , 4675 —4684.