Solvent-free synthesis and key intermediate isolation in Ni_2Dy_2 catalyst development in the domino ring-opening electrocyclization reaction of furfural and amines

Stavroula I. Sampani,[a] Andrew McGown,[a] Alfredo Vargas, [a] Alaa Abdul-Sada,[a] Graham J. Tizzard,[b] Simon J. Coles,[b] John Spencer [a] and George E. Kostakis[a]*

[a]*Department of Chemistry, School of Life Sciences, University of Sussex, Brighton BN1 9QJ, UK. E-mail: G.Kostakis@sussex.ac.uk*

[b]*UK National Crystallography Service, Chemistry, University of Southampton, SO1 71BJ, UK*

ABSTRACT

A solvent-free methodology that yields *trans*-4,5-diaminocyclopent-2-enones, main domains of natural products and variety of N-heterocycles, is described. The bimetallic catalyst $[Ni^{II}_2Dy^{III}_2L_4(DMF)_6]$ 2(OTf) 2(DMF) (**1**) promotes the domino reaction of furfural and amines, with loadings as low as 0.01%, under stirring or microwave assisted conditions to afford the corresponding frameworks in very good to excellent yields. Crystallographic and theoretical

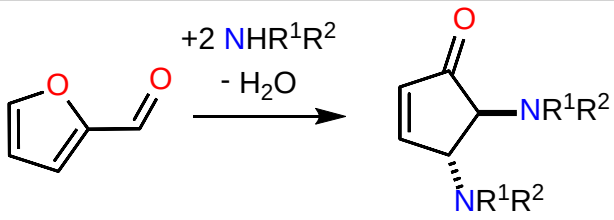
studies shed light on the exclusive formation of the *trans*-diastereoisomers via a 4π-conrotatory electrocyclization process elucidating the key step in the catalytic process.

INTRODUCTION

New synthetic methodologies that reduce our dependence on fossil fuels and rare elements are highly profilic in current synthetic chemistry.[1–6] Furfural, or 2-furaldehyde, is a biomass derivative produced in million-ton quantities annually.[7] The availability and ready affordability of this framework are compelling factors for its use to access high-value core building blocks,[8–11] although the development of various methodologies to convert this oxygen-rich skeleton into building blocks for use in pharmaceuticals is required. On the other hand, bimetallic catalysts have been recognized as a powerful tool for molecular transformations enabling energy-efficient one-pot reactions as an alternative to multi-step protocols or achieving high enantioselectities.[12–17] We initiated a project toward the development of well-characterized 3d/4f bimetallic coordination entities that remain intact in solution and efficiently promote a series of organic transformations.[18–22] The precise topology of these entities, the partially saturated coordination geometry of each metal center and in particular the distance separating the metals have been suggested to be key parameters for efficient catalysis.[12,13] The presence of two different metals with significantly different binding selectivity (3d vs 4f), promotes the selective substrate binding; this is a significant advantage compared to homometallic catalysts. Additionally, the 4f centers retain their catalytic activity in the presence of Lewis basic N-groups allowing their use with unprotected amines,[23] whereas the 3d centres can be redox active[24,25] or promote other transformations.[26]

In 2007, Batey reported a methodology that yielded *trans*-4,5-diamino-2-cyclopentenones (Scheme 1) and involved furfural, secondary amines and $Dy(OTf)_3$ as the promoter.[27] This organic

transformation proceeds via a domino ring-opening/4π-electrocyclization pathway with only one equivalent of water generated as a side product.[28–31] This organic framework can be found in several natural products and thereafter several efficient methodologies that promote the synthesis of racemic, *trans*-4,5-diamino-2-cyclopentenones have been developed and recently reviewed.[32–36] The methodology reported by Nardi proceeds in water and is microwave assisted, ,[35] whilst immobilized alternates have been reported.[37] However, in both occasions the protocols have moderate performance when primary amines are used therefore, the development of alternative methodologies is required.



Reference	Promoter	Loading	Solvent	Temperature	Time
2007, [27]	$Dy(OTf)_3$	10%	CH_3CN	r.t.	16 h
2013, [34]	$ErCl_3\ 6H_2O$	0.1%	Ethyl lactate	r.t.	30 min
2013, [36]	$AlCl_3$	10%	CH_3CN	r.t.	5 h
2015-**16**,[38,39]	$Ni_2Ln_2L_4Cl_2$	1%	CH_3CN	r.t.	2 h
2017, [37]	$ErCl_3\ 6H_2O$ on silica	10%	n-butanol	r.t.	30 min
2017, [35]	no catalyst		H_2O	MW 60°C	40 min
2018, [33]	$Cu(OTf)_2$	1%	H_2O	r.t.	10 min
This work,	$\{Ni_2Dy_2L_4\}^{2+}$ 2(OTf)	0.01%	solvent-free	r.t.	40 min
This work,	$\{Ni_2Dy_2L_4\}^{2+}$ 2(OTf)	0.01%	solvent-free	MW 60°C	10 min

Scheme 1. Reported methodologies employing metal based Lewis acids and MW techniques.

We demonstrated that the bimetallic tetranuclear $Ni^{II}_2Ln^{III}_2$[38,39] entity shows remarkable catalytic activity in the reaction of furfural and secondary or primary amines to yield *trans*-4,5-diaminocyclopent-2-enones or the corresponding and very well-known Stenhouse salts,[40,41] respectively. We identified that treatment of Stenhouse salts under acidic conditions (silica gel or diluted HCl solution) yields the corresponding ring-closed product. Moreover, we identified a

negligible contribution of the Ni^{II} moiety in the transformation confirming that the domino reaction is driven solely by the 4f ion, whilst functionalization of the organic skeleton (second coordination sphere effects) is feasible without lowering the catalytic efficacy. Our methodology is industrially appealing as it allows the reaction to proceed under air and provides the expected framework with secondary and primary amines and therefore being the only actual competent to the expensive $Sc(OTf)_3$.[27] However, considering the aza-Piancatelli transformation as an excellent paradigm for sequential bimetallic catalysts to provide a wide range of nitrogen-based heterocycles,[42] it was of high importance to optimize our synthetic methodology before proceeding to more complex reactions. Therefore, capitalizing on our preliminary findings and considering the recent advances of this reaction,[32] we report herein the development of our synthetic protocols and identify their applicability.

RESULTS & DISCUSSION

Considering the efficiency of triflate anions in organic transformations,[43] the recently reported reusable implementation of $Cu(OTf)_2$[33] in yielding *trans*-4,5-diaminocyclopent-2-enones, as well the enhanced stability in solution of the tetranuclear defect dicubane Ni_2Ln_2 framework, we envisaged that the corresponding triflate analogue of the previously reported $Ni_2Ln_2Cl_2$ series would serve as an ideal promoter of this reaction. $[Ni_2Dy_2L_4(DMF)_6]$ 2(OTf) 2(DMF) (**1**) can be synthesized in two high yielding steps (97% total yield) under ambient conditions and commercial starting materials. The first step involves the near quantitative synthesis of the ligand (*E*)-2-(((2-hydroxyphenyl)imino)methyl)-6-methoxyphenol (H_2L) from the condensation reaction between *o*-vanillin and 2-aminophenol. Ligand H_2L is incorporated in the synthesis of the previously developed bimetallic entities $Ni^{II}_2Ln^{III}_2$.[38,39] The ligand then is involved in a room temperature reaction with $Ni(OTf)_2$ and $Dy(OTf)_3$ in a ratio (2:1:1), in absence of a base, to yield yellow-green

crystalline material. Single X-Ray crystallographic studies identified the structure of **1** as shown in Figure 1. The four organic ligands partially saturate the coordination environment of all metal centers (five out of six and six out of eight for Ni and Dy, respectively), whilst the remaining positions are occupied by exchangeable solvent DMF molecules, forming thus the dicationic robust framework $\{Ni_2Dy_2L_4(DMF)_6\}^{2+}$. The two lattice OTf anions balance the charge, whilst ESI-MS data show peaks that can be attributed to the "naked-solvent free" dicationic $[Ni^{II}_2Dy^{III}_2L_4]^{2+}$ core; this core remains intact in a series of protic and polar organic solvents such as MeOH, EtOH, DMF, CH_3CN and H_2O. Compound **1** was further characterized by elemental analysis, UV-Vis and thermogravimetric analysis (Figures S1 – S4).

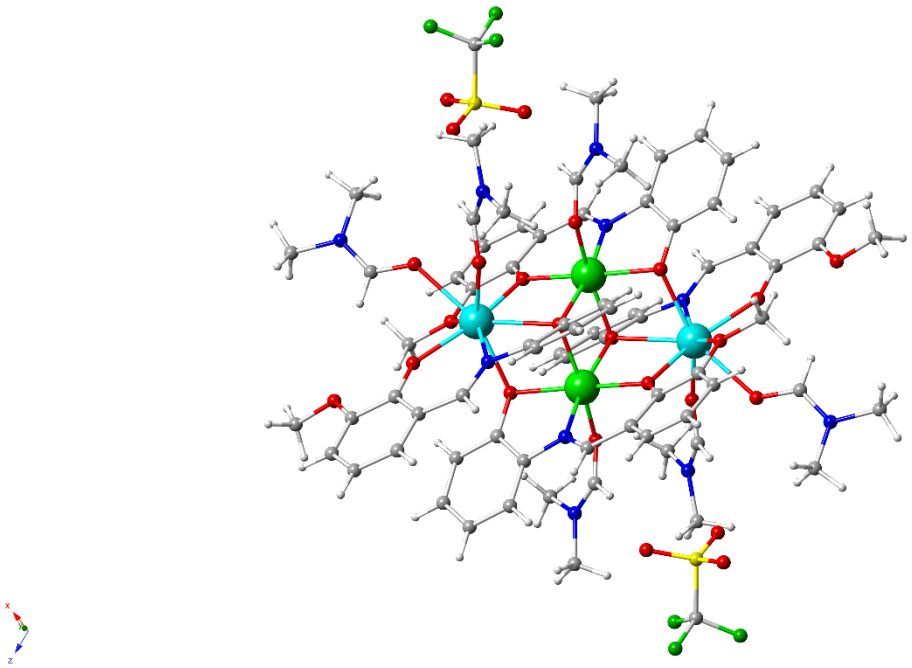
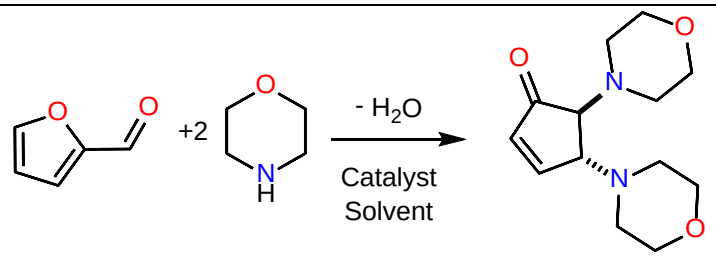


Figure 1. Molecular structure of $[Ni_2Dy_2L_4(DMF)_6]$ 2(OTf) 2(DMF) , **1**. Color code: Ni^{II}: green; Dy^{III}: light blue; O: red; N: blue; C: grey; F: light green; S: yellow. Hydrogen atoms and lattice DMF molecules are omitted for clarity.

Table 1. Comparison of catalytic activity for compound **1**.



Entries	Catalyst	*T*	Loading [%]	Time	Yield of **2a** %[a]
1	$Dy(OTf)_3$	25ºC	10	24 hours	Quantitative[27]
2	$Ni_2Dy_2Cl_2$	25ºC	1	2 hours	Quantitative[39]
3	**1**[b]	25ºC	1	60 min	>99
4	**1**[b]	25ºC	0.1	60 min	>99
5	**1**[b]	25ºC	0.01	60 min	>99
6	$Ni_2Dy_2Cl_2$[b]	25ºC	0.01	40 min	40
7	**1**[c]	25ºC	0.01	40 min	93
8	**1**[c]	25ºC	0.005	40 min	70
9	**1**[d]	60ºC (MW)	0.01	10 min	95

[a] Determined by ^{1}H NMR spectroscopy.
[b] Reaction conditions: amine, 1.1 mmol; 2-furaldehyde, 0.5 mmol; 4Å MS 100 mg; anhydrous EtOAc 2 mL; room temperature; Catalyst loading calculated per equivalent of Dy.;
[c] Reaction conditions : Stirring 40min, Solvent – free, amine, 2.2 mmol; 2-furaldehyde, 1 mmol; 4Å MS; Catalyst loading 0.01% (calculated per equivalent of Dy).
[d] Reaction conditions : Microwave 10min, Solvent – free, amine, 2.2 mmol; 2-furaldehyde, 1 mmol; 4Å MS; Catalyst loading 0.01% (calculated per equivalent of Dy).

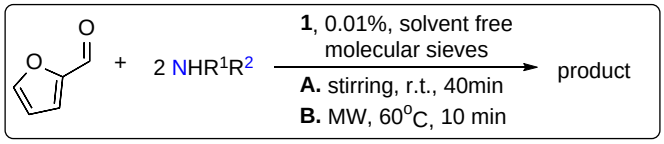
With the catalyst in hand and aiming to further develop our protocols, we selected EtOAc, considered as a solvent with an enhanced "green" character,[44] in the reaction between 2-furaldehyde and morpholine. Following the reported protocols (Table 1, entries 1 & 2), the catalytic reaction with 1% loading of **1** yielded the corresponding framework in a quantitative amount in 40 minutes (Table 1, entry 3), whilst reactions conducted with one and two orders of magnitude lower catalyst loadings (0.1% and 0.01%) were equally found to be efficient (Table 1, entries 4 and 5). When compared with the prototype catalyst, $Dy(OTf)_3$ (Table 1, entry 1),[27] our protocol proceeds with three orders of magnitude less catalyst loading, whereas a reaction under

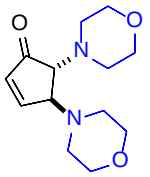
similar conditions with $Ni_2Dy_2Cl_2$ yielded the corresponding framework in 40% yield. This result identifies the important role of the OTf anion in the transformation (Table 1, entry 6). However, aiming to develop a greener protocol and having in mind that the transformation is promoted by acidic ionic liquids under solvent-free conditions,[45] we attempted a solvent-free reaction with a catalyst loading of 0.01% (Table 1, entry 7,). To our delight, the reaction proceeded in excellent yield within 40 minutes, whilst a further decrease in catalyst loading to 0.005% can afford the ring closed product in 70% yield (Table 1, entry 8). Finally, considering the recent developments in the atom-efficient domino condensation/ring-opening/electrocyclization reaction[35] and that the use of microwaves[46] is a very effective technique that facilitates the synthesis by significantly reducing the time, we attempted a solvent-free reaction under microwave conditions. To our delight, the solvent-free reaction proceeds in excellent yields in only 10 minutes and catalyst loadings of 0.01% (Table 1, entry 9). The methodologies involving stirring or microwave conditions are named thereafter as "**A**" and "**B**", respectively.

We then explored the scope of the reaction by employing a variety of secondary amines as substrates (Table 2, compounds **2b** – **2d**) and isolating the corresponding products in very good to excellent yields, with methodology B having a slightly better performance. The use of **1**, as a catalyst, in the reaction of furfural and primary amines yields the corresponding deprotonated Stenhouse salts (Table 2, compounds **3a** – **3d**).[38,39] This result is in line with our previous findings and in contrast to the use of $Cu(OTf)_2$[33] and $Dy(OTf)_3$[27] as catalysts, in which the synthesis of the corresponding Schiff base or no reactivity is observed, respectively. This difference supports the applicability of our catalyst and methodology and justifies our choice in further investigating its catalytic efficacy. The ring closing of the zwitterion to the corresponding cyclopentanones proceeds under acidic conditions, as we have shown before,[38,39] and is independent of the Dy

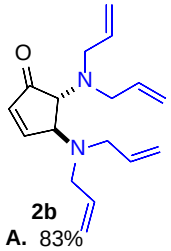
moiety but dependent on the electron withdrawing substitution in aromatic primary amines; i.e. treatment of **3d** under acidic conditions does not afford the corresponding ring-closed product.

Table 2. The scope of the reaction of secondary amines and primary amines with furfural, promoted by **1** under solvent-free conditions, stirring (**A**) and MW (**B**).

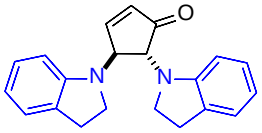




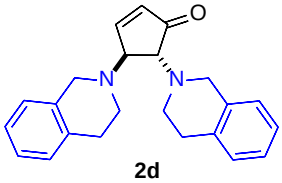
2a
A. 93%
B. 95%



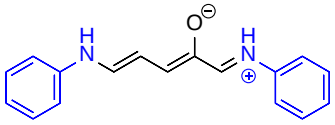
2b
A. 83%
B. 83%



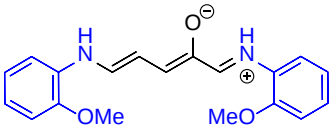
2c
A. 89%
B. 95%



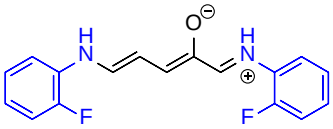
2d
A. 80%
B. 89%



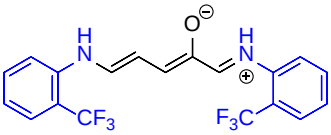
3a
A. >99%
B. >99%



3b
A. 85%
B. 95%



3c
A. 91%
B. 94%

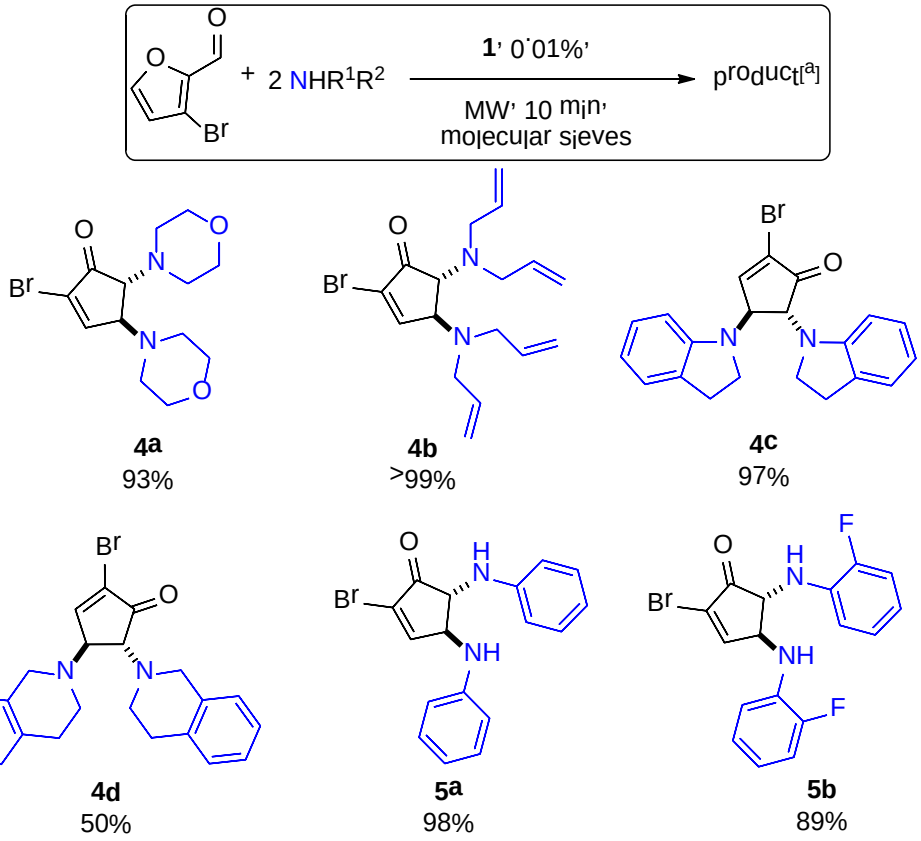


3d
A. 69%
B. 88%

Method A. Reaction conditions : Stirring 40min, Solvent – free, amine, 2.2 mmol; 2-furaldehyde, 1 mmol; 4Å MS; Catalyst loading 0.01% (calculated per equivalent of Dy). Method B. Reaction conditions : Microwave 10min, Solvent – free, amine, 2.2 mmol; 2-furaldehyde, 1 mmol; 4Å MS; Catalyst loading 0.01% (calculated per equivalent of Dy).

To further identify the versatility of our protocol for this transformation, we incorporated 3-bromofurfural instead of furfural (Table 3). This has been suggested as an ideal pathway to afford 2-bromo *trans*-4,5-diaminocyclopent-2-enones, which can then be transformed into natural product-like scaffolds.[47] The reaction proceeds in the presence of the minimum amount of CH_3CN or EtOAc as a solvent to solubilize the substituted furfural moiety and achieves very good to excellent yields with almost three orders of magnitude less catalyst loading when compared to the state-of-the-art for this domino reaction.[47] The reaction of morpholine or aniline with 3-bromofurfural, in absence of molecular sieves, yielded the corresponding morpholinium bromide[48] and anilinium bromide,[49] as it was confirmed by single X-Ray studies. This outcome indicates that the reaction is highly sensitive and limited from the presence of water; therefore, other developed microwave assisted methodologies[35] are not suitable to promote this specific type of transformation.

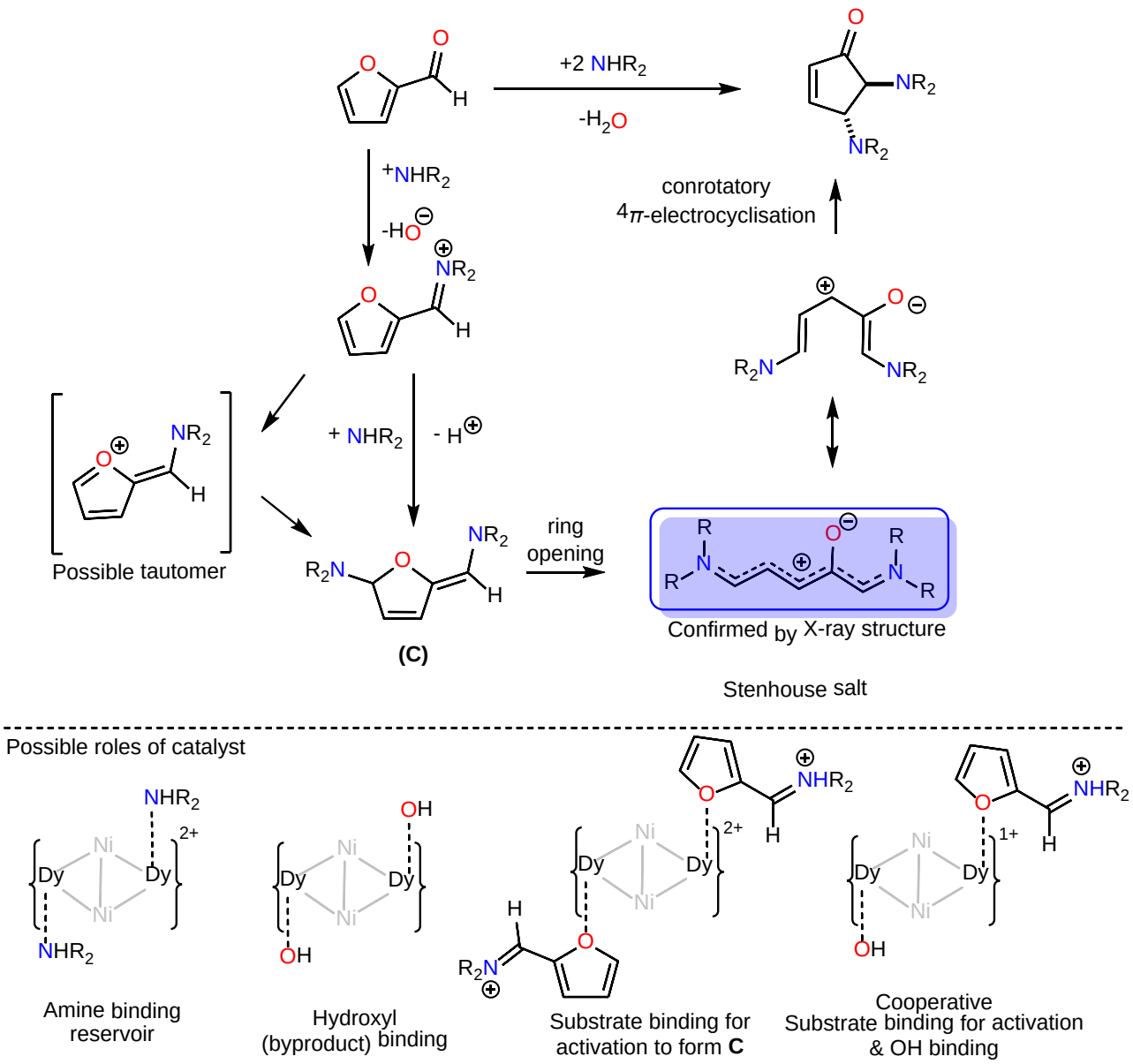
Table 3. The scope of the reaction with 3-bromo-2-furaldehyde, promoted by **1** under MW conditions.



[a]Condition: Microwave 10min, Solvent CH_3CN (100 µL to solubilise the aldehyde), amine, 2.2 mmol; aldehyde, 1 mmol; 4Å MS; Catalyst loading 0.01% (calculated per equivalent of Dy).

Previous theoretical studies by us,[39] identified that the pathway from the Stenhouse salt to the final product (Scheme 2) is highly favorable, indicating that the catalysis takes place prior to this step, and the total electronic energy of intermediate **C** (Scheme 2) concerns a pyramidal-to-planar evolution of the beta-nitrogen, a key feature that is likely involved in the catalytic process. In our quest to shed light on the chemical transformation, we attempted to isolate an intermediate Stenhouse salt of the reaction between furfural and aniline (**3a**). Short-living light red needle-

shaped crystals are formed when dilute HCl is added directly to the NMR tube of the crude product, thereafter the crystals are named **3a HCl**. The X-Ray study confirms the isolation of the intermediate with two crystallographically independent entities. The five carbon atoms (C7-C11 result of the ring opening of the furfural) are in a linear configuration. Bond distances (Table 4) and the freely refined H- atoms provide the following four valuable insights regarding the intermediate. A) The two carbon-nitrogen bonds (Entries 1 & 3, Table 4) are significantly shorter than the corresponding $C_{aromatic}$-N bonds (Entries 2 & 4, Table 4). Single (C – N) or double (C = N) bonds of reported aniline-based compounds are in the range of 1.434 – 1.472 Å [50,51] and 1.260 – 1.278Å,[52,53] indicating the hybrid intermediate (single/double) character of the (N1-C7, N2-C11) bonds. B) The four C – C (Entries 5 – 8, Table 4) bonds are in the borderline between a single and double bond and have similar values with the aromatic ring (Entries 9 – 12, Table 4). C) The C – O bond (Entries 13 & 14, Table 4) is at 1.375(7) Å or 1.402(6) Å (56/44 ratio) which is indicative of a single bond, whilst the O atom is protonated. D) The freely refined H-atoms in the four C and two N atoms exclude a sp^3 configuration. All these notes indicate the best described confirmation is the delocalized scheme shown in Figure 2. A survey in the crystallographic database (CSD)[54] for derivatives based on furfural and amines yielded in no results, therefore we may propose that **3a HCl** is the first crystallographically isolated Stenhouse salt example.



Scheme 2. A proposed mechanism incorporating the key intermediate characterized in this study and possible roles of catalyst according to the literature.[55]

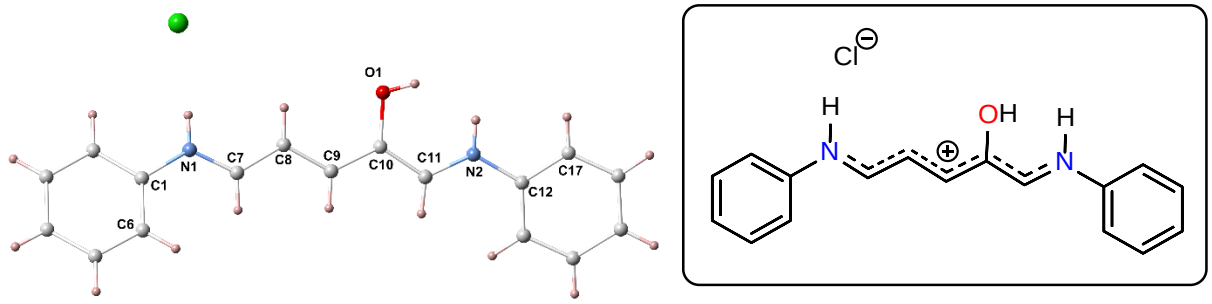


Figure 2. A crystallographic (left) and schematic (right) representation of the intermediate **3a HCl**. Color code C (Grey), N (light blue), O(red), Cl (green)

Table 4. Selected Bond Distances (Å) for N – C, C – C and C – O bonds in compound **3a HCl**.[a]

Entries	First entity			Second entity		
1	N1	C7	1.333(5)	N51	C57	1.331(5)
2	N1	C1	1.406(5)	N51	C51	1.411(5)
3	N2	C11	1.332(5)	N52	C61	1.335(5)
4	N2	C12	1.402(5)	N52	C62	1.409(5)
5	C8	C7	1.376(5)	C58	C59	1.387(5)
6	C8	C9	1.389(6)	C58	C57	1.385(6)
7	C10	C9	1.385(5)	C61	C60	1.373(6)
8	C10	C11	1.385(6)	C59	C60	1.386(6)
9	C1	C6	1.388(6)	C62	C67	1.386(6)
10	C1	C2	1.394(6)	C62	C63	1.388(6)
11	C12	C13	1.380(6)	C51	C52	1.384(6)
12	C12	C17	1.386(6)	C51	C56	1.387(6)
13	C10	O1B	1.375(7)	C58	O51A	1.375(6)
14	C8	O1A	1.402(6)	C60	O51B	1.412(8)

[a] Two crystallographic identical entities can be found in the crystal structure of **3a HCl**, however only first entity is drawn in Figure 2.

We sought to put into context the 'position' of the observed planar intermediate within the transformation frame by considering the electronic structure, geometry and both quantitative and qualitative metrics based on partial charges, molecular electrostatic potentials and molecular orbitals (MO). Hence, calculations were carried out based on Kohn-Sham density functional theory

(DFT) at the OLYP/TZ2P level. Table S2 indicates selected bond distances for different zwitterionic forms of the intermediate (**3a HCl**, **3a**$^{+}$ and **3a**) and one transition state **3a TS** in which the aryl next to nitrogen is perpendicular to the molecular plane. Table S3 shows Hirshfeld charge at some selected atom centers. Figure S6 shows the frontier orbitals of **3a** and the other forms. As with the X-ray structure, the calculations present a highly planar geometry for **3a**. This stems from the highly conjugated C-C framework between the two N atoms as can be seen in Figure 3 and this is observed for all forms, that is, the overall (planar) structure is not affected whether the molecule is neutral, protonated, or in the presence of counter-ion; importantly, this feature is also present in the transition state. Some differences start to appear when considering the partial charges, though this just mainly reflect the fact that in both **3a** and **3a TS** the oxygen is anionic. A further similarity between the latter two is shown by the Coulombic molecular electrostatic potential as mapped on the surface density as shown in Figure S7. However, where the important distinction lies is in the overall electronic energy; Figure 4 shows the energetic profiles of the **3a**, **3a TS** and the Stenhouse salt. Results suggest that the twisting of the aryl next to N2 is the first step towards cyclisation, this step already puts the system to 40% of the energy required to attain the non-linear structure. We conclude that the planar intermediate is a key step in the catalysis and the conjugation it bears plays a major role, that is, it is highly stable but an induced slight variation in its geometry pushes it easily towards to the observed reaction products.

Taking into account : a) the reaction takes place in solvent free conditions, b) the partially saturated coordination environment of the Dy centers, c) the rigidity of the tetrametallic unit as well its possibility to exchange solvent molecules, d) kinetic studies in which the $Dy(OTf)_3$ catalyzed aza-Piancatelli rearrangement is controlled by a key off-cycle binding between aniline and Dy,[55] and e) the oxophilic character of the Dy moiety, that may either bond to hydroxyl group

HO^- (byproduct trap), substrate (activation) or both, we propose a mechanism of the 4π-conrotatory electrocyclization process (Scheme 2) that involves the bimetallic entity. Such an observation, we believe, provides valuable insight into the full detailed mechanism of the reaction, attempts to understand the detailed role of the bimetallic catalyst as well may explain the reactivity of the bimetallic system at very low loadings.

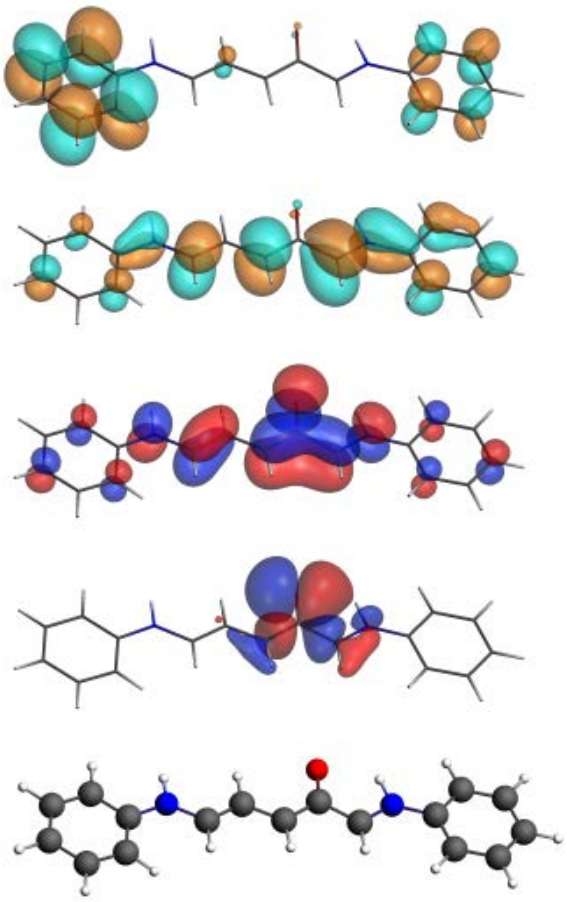


Figure 3. Calculated structure and frontier orbitals of **3a**. The two MOs in the top are the lowest unoccupied, whilst the two MOs in the bottom are the highest occupied. A bond stick model is given for clarity.

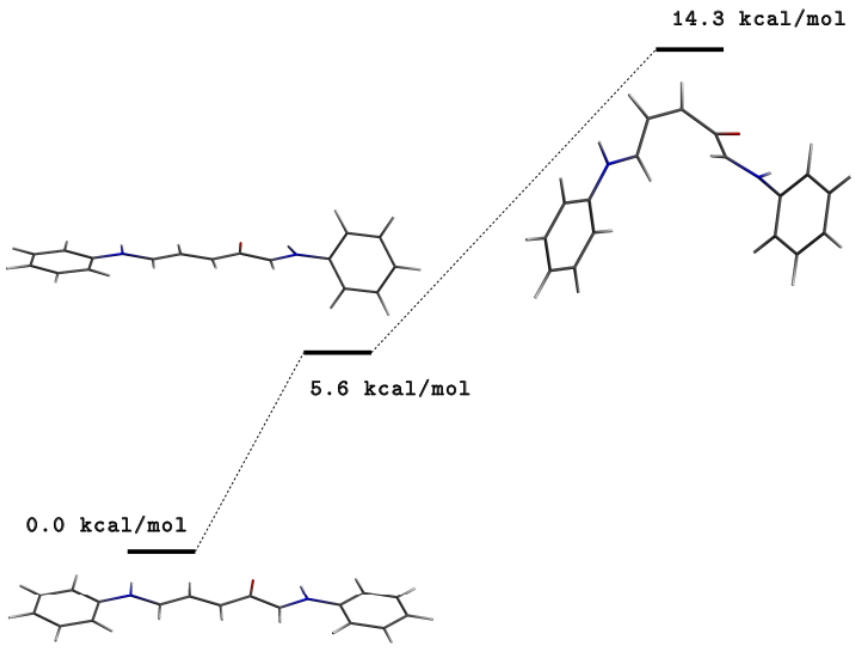


Figure 4. Energy profile of the planar **3a** going to the perpendicular aryl bearing **3a TS** and finally towards the Stenhouse salt

Conclusions

We report herein an efficient synthetic methodology that yields, in a diastereoselective manner, *trans*-4,5-diaminocyclopent-2-enones. Developing our previous methodology, the triflate analogue of the tetranuclear Ni_2Ln_2 moiety (**1**), enhances the catalytic efficacy of the bimetallic catalyst by two orders of magnitude and when compared with state-of-the-art catalysts of this reaction this attains two[33] or three[27] orders of magnitude in terms of improvements. Moreover, our effort to identify environmental friendly protocols showcased that the reaction can take place in EtOAc as a solvent, however, excellent yields are obtained when solvent-free, stirring or microwave assisted, conditions are followed. The developed methodology is applicable to a series of secondary and primary amines as well the substituted 3-bromofurfulaldehyde, yielding the

corresponding frameworks. The first crystallographic characterization of the Stenhouse salt intermediate supports the exclusive formation of the *trans*-diastereoisomers via a 4π-conrotatory electrocyclization. Theoretical studies shed light on the formation of the planar intermediate and suggest the latter to be a key step in the catalytic process. The optimized present catalytic protocol paves the way to use **1** or its derivatives as dual/tandem catalysts in other organic transformations and this is an ongoing research task in our laboratory.

Experimental Section

Materials.

All reagents were purchased from Sigma Aldrich, Fluorochem, Tokyo Chemical Industry, Apollo Scientific, Fischer Scientific or Alfa Aesar and used without further purification. All experiments were performed under aerobic conditions.

Instrumentation.

NMR spectra were recorded with a Varian VNMRS 500 or Varian VNMRS 600 at 30 °C on solution-state samples in $CDCl_3$ or DMSO-d_6.Chemical shifts are quoted in parts per million (ppm). Coupling constants (J) are recorded in units of Hz. IR spectra were recorded over the range of 4000–650 cm^{-1} on a PerkinElmer Spectrum One FT-IR spectrometer fitted with a UATR polarization accessory. HRMS (ESI- FTMS) data were obtained on a VG Autospec Fissions instrument (EI at 70 eV) and carried out by Dr A. K. Abdul-Sada at the University of Sussex. Thermogravimetric analysis was carried out with a Thermogravimetric analyser Q-50 V20.13 using a platinum pan, in a nitrogen atmosphere from 25 – 792 °C. UV-Vis spectra were collected for the coordination cluster and its ligand using NanoDrop spectrophotometry. Elemental analysis

was performed at London Metropolitan University. The synthesis reported involving the use of microwave irradiation was performed in a CEM Discover SP microwave reactor unit with CEM Explorer Microwave auto sampler and undertaken using CEM 10 ml sealed microwave reactor vials with PTFE caps. An internal infrared probe was utilized to monitor and control the temperature of the reaction allowing for precise and reproducible reaction conditions.

Ligand synthesis.

The ligand (E)-2-(((2-hydroxyphenyl)imino)methyl)-6-methoxyphenol (H_2L) was synthesized following previous procedure.[38]

Catalysts synthesis.

$[Ni^{II}_2Dy^{III}_2L_4(DMF)_6]$ 2(OTf) 2(DMF) (**1**) was synthesized by the following procedure: H_2L (0.2 mmol, 48 mg), $Dy(OTF)_3$(0.1 mmol, 61 mg) and $Ni(OTF)_2$ (0.1 mmol, 36 mg) were added in EtOH (20 mL) and the resulting mixture was stirred for 1 hour. During this time, a yellow precipitate was formed from the yellow solution. The precipitant was filtered off, then washed with cold EtOH (20 mL) and Et_2O (10 mL) and dried in vacuum. The precipitate (**1**) was then collected and crystallised in DMF and Et_2O, forming yellow-greenish crystals. Yield = 95%, based on Dy. Elemental analysis for $Ni_2Dy_2C_{74}H_{86}N_{10}O_{18}(CF_3SO_3)_2(C_3H_7NO)_2$: C 42.96, H 4.40, N 7.34; found C 42.62, H 4.51, N 7.13.

General Catalytic Protocol.

Compounds 2a-2d and 3a-3d.

A capped vial equipped with a magnetic stirbar, aldehyde (1 mmol), amine (2.2 mmol) 3mg of catalyst (0.01% total of Dy) were added. The resultant mixture was (method A) stirred at room temperature for 40 minutes (method B) placed under microwave irradiation at 60◦C for 10 mins. The (cooled to ambient temperature, in the case of (B)) reaction mixture was diluted with CH_2Cl_2 (DCM) (20 mL) and filtered through Celite. The resultant solution was concentrated under reduced pressure and the residue purified by column chromatography (ethyl acetate in hexanes), according to the previously reported procedure.[38] The products were obtained as red or yellow oils, which solidified on standing.

Compounds 4a-4d and 5a-5b.

A capped vial equipped with a magnetic stirbar. MeCN (dry, 100μL), aldehyde (1 mmol), amine (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture underwent microwave irradiation at 60◦C for 10 mins. The reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solution was concentrated under reduced pressure and the residue purified by column chromatography (ethyl acetate in hexanes). The products were obtained as red or yellow oils, which solidified on standing.

***trans*-4,5-Dimorpholin-4-yl-cyclopent-2-enone (2a)**

A capped vial equipped with a magnetic stirrer, furfural (1 mmol), morpholine (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture (method A) was stirred at room temperature for 40 minutes (method B) underwent microwave irradiation at 60◦C for 10 mins. In each case, the (cooled for method B) reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solutions by methods A and B were concentrated under reduced pressure and the residues were purified by column chromatography (30% ethyl acetate in

70% hexane), according to the previously reported procedure.[38] The product by each method was obtained as yellow oil, which solidified on standing. Method A provided the sample whose purity is documented by NMR. ^{1}H NMR (500MHz, $CDCl_3$) δ 7.59 (1H, dd, *J* = 6.0, 2.0 Hz), 6.22 (1H, dd, *J* = 6.0, 2.0Hz), 3.79 (1H, ddd, *J* = 3.0, 2.0, 2.0 Hz), 3.71 (4H, t, *J* = 4.5 Hz), 3.67 (4H, t, *J* = 4.5 Hz), 3.28 (1H, d, *J* = 3.0 Hz), 2.84-2.79 (2H, m), 2.67-2.55 (6H, m), ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 206.3, 160.8, 135.6, 68.3, 67.5, 67.3, 66.9, 66.9, 60.3, 50.3, 50.1. (Method A) conversion 93%, (method B) conversion 95%; (method A) isolated yield = 232 mg, 92%, (method B) isolated yield = 235 mg, 93%.

***trans*-4,5-bis(Diallylamino)cyclopent-2-enone (2b)**

Capped vial equipped with a magnetic stirrer, furfural (1 mmol), diallylamine (2.2 mmol) and 3 mg (0.01% total of Dy) were added. The resultant mixture (method A) was stirred at room temperature for 40 minutes (method B) underwent microwave irradiation at 60◦C for 10 mins. In each case, the (cooled for method B) reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solutions by methods A and B were concentrated under reduced pressure and the residues were purified by column chromatography (5% ethyl acetate in 95% hexane), according to the previously reported procedure.[38] The product by each method was obtained as yellow oil, which solidified on standing. Method A provided the sample whose purity is documented by NMR. ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.46 (1H, dd, *J* = 6.0, 2.0 Hz), 6.16 (1H, dd, *J* = 6.0, 2.0 Hz),5.91-5.77 (4H, m), 5.26-5.10 (8H, m), 4.11 (1H, ddd, *J* = 3.0, 2.0, 2.0 Hz), 3.59 (1H, d, *J* = 3.0Hz), 3.38-3.31 (2H, m), 3.23-3.10 (6H, m), ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 207.9, 162.6, 136.7, 136.3, 135.0, 117.6 (2 peaks), 65.2, 63.7, 54.6, 53.8. (Method A) conversion 83%, (method B) conversion 83%; (method A) isolated yield = 215 mg, 79%, (method B) isolated yield = 212 mg, 78%.

***trans*-4,5-bis-(2,3-Dihydroindol-1-yl)-cyclopent-2-enone (2c)**

A capped vial equipped with a magnetic stirrer, furfural (1 mmol), indoline (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture (method A) was stirred at room temperature for 40 minutes (method B) underwent microwave irradiation at 60◦C for 10 mins. In each case, the (cooled for method B) reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solutions by methods A and B were concentrated under reduced pressure and the residues were purified by column chromatography (20% ethyl acetate in 80% hexane), according to the previously reported procedure.[38] The product by each method was obtained as yellow oil, which solidified on standing. Method A provided the sample whose purity is documented by NMR. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (1H, dd, *J* = 6.0, 2.0 Hz), 7.08 (1H, d, *J* = 7.0 Hz), 7.05 (1H, d, *J* = 7.5 Hz), 6.96 (1H, dd, *J* = 7.5, 7.5 Hz), 6.91 (1H, dd, *J* = 7.5, 7.5 Hz), 6.67 (1H, dd, *J* = 7.5, 7.5 Hz), 6.63(1H, dd, *J* = 7.5, 7.5 Hz), 6.49 (1H, dd, *J* = 6.0, 2.0 Hz), 6.35 (1H, d, *J* = 8.0 Hz), 6.07 (1H, d, *J* =8.0 Hz), 5.01-4.99 (1H, m), 4.40 (1H, d, *J* = 3.5 Hz), 3.52 (1H, ddd, *J* = 7.5, 7.5, 7.5 Hz), 3.50(1H, ddd, *J* = 8.0, 8.0, 8.0 Hz), 3.41 (1H, ddd, *J* = 8.0, 8.0, 8.0 Hz), 3.34 (1H, ddd, *J* = 8.0, 8.0,8.0 Hz), 3.06-2.90 (4H, m), ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 192.1, 159.3, 150.8, 150.6, 129.4, 128.9, 127.4, 124.6, 123.7, 117.8, 117.3, 107.5, 106.7, 62.2, 58.2, 53.1, 49.5, 48.4, 40.5, 27.8, 27.7. (Method A) conversion 89%, (method B) conversion 95%; (method A) isolated yield = 269 mg, 85%, (method B) isolated yield = 294 mg, ***trans*-4,5-Bis-(3,4-dihydro-*1H*-isoquinolin-2-yl)-cyclopent-2-enone (2d)**

A capped vial equipped with a magnetic stirbar, furfural (1 mmol), 1,2,3,4- tetrahydroisoquinoline (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture (method A) was stirred at room temperature for 40 minutes (method B) underwent microwave irradiation at 60◦C for 10 mins. In each case, the (cooled for method B) reaction mixture was diluted with

DCM (20 mL) and filtered through Celite. The resultant solutions by methods A and B were concentrated under reduced pressure and the residues were purified by column chromatography (30% ethyl acetate in 70% hexane), according to the previously reported procedure.[38] The product by each method was obtained as yellow oil, which solidified on standing. Method A provided the sample whose purity is documented by NMR. ^{1}H NMR (500 MHz, CDCl3) δ 7.70 (1H, dd, *J* = 6.0, 2.0 Hz), 7.16-7.00 (8H, m), 6.32 (1H, dd, *J*=6.0, 2.0 Hz), 4.25-4.13 (2H, m), 3.95-3.90 (3H, m), 3.62 (1H, d, *J* = 3.0 Hz), 3.12-2.86 (8H,m), ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 207.0, 161.4, 135.4, 135.1, 134.5, 134.4, 134.2, 128.9, 126.6, 126.5, 126.4, 126.0, 125.8, 125.6, 67.9, 67.4, 53.0, 52.4, 47.5, 47.4, 30.3, 29.8. (Method A) conversion 80%, (method B) conversion 89%; (method A) isolated yield = 258 mg, 75% (method B) isolated yield = 299 mg, 87%.

(*1E,2Z,4E*)-5-(Phenylamino)-1-(phenyliminio)penta-2,4-dien-2-olate (3a)

A capped vial equipped with a magnetic stirrer, furfural (1 mmol), aniline (2.2 mmol) and the appropriate amount of catalyst (0.01% total of Dy) were added. The resultant mixture (method A) was stirred at room temperature for 40 minutes (method B) underwent microwave irradiation at 60◦C for 10 mins. In each case, the (cooled for method B) reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solutions by methods A and B were concentrated under reduced pressure and the residues were purified by column chromatography (10% ethyl acetate in 90% hexane), according to the previously reported procedure.[38] The product by each method was obtained as red oil, which solidified on standing. Method A provided the sample whose purity is documented by NMR. ^{1}H NMR (500 MHz, DMSO-*d6*) δ 7.68 (dd, *J* = 6.1, 1.9 Hz, 1H), 7.11 – 7.01 (m, 4H), 6.63 – 6.44 (m, 6H), 6.39 (dd, *J* = 6.1, 1.5 Hz, 1H), 6.20 (d, *J* = 8.6 Hz, 1H), 6.06 (d, *J* = 7.5 Hz, 1H), 4.63 – 4.57 (m, 1H), 4.01 (dd, *J* = 7.6, 3.4 Hz, 1H), 1.22 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-*d6*) δ 205.1, 161.9, 152.4, 151.6, , 132.6, 129.7, 129.5, 129.2,

126.5, 121.3, 117.3, 116.7, 116.1, 114.36, 113.17, 112.9, 64.9. (Method A) conversion>99%, (method B) conversion>99%; (method A) isolated yield = 256 mg, 97%, (method B) isolated yield = 256 mg, 97%.

(1E,2Z,4E)-5-((2-Methoxyphenyl)amino)-1-((2-methoxyphenyl)iminio)penta-2,4-dien-2-olate (3b)

A capped vial equipped with a magnetic stirrer, furfural (1 mmol), o-anisidine (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture (A) was stirred at room temperature for 40 minutes (B) underwent microwave irradiation at 60◦C for 10 mins. In each case, the (cooled for B) reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solutions by methods A and B were concentrated under reduced pressure and the residues were purified by column chromatography (10% ethyl acetate in 90% hexane), according to the previously reported procedure.[38] The product by each method was obtained as red oil, which solidified on standing. Method A provided the sample whose purity is documented by NMR. ^{1}H NMR (500 MHz, DMSO-*d6*) δ 8.35 (s, 1H), 7.61 (dt, *J* = 6.1, 1.7 Hz, 2H), 7.29 – 7.17 (m, 2H), 7.07 (d, *J* = 7.8 Hz, 1H), 7.02 – 6.94 (m, 3H), 6.89 – 6.69 (m, 19H), 6.55 (dt, *J* = 3.5, 1.7 Hz, 1H), 6.41 (dt, *J* = 6.1, 1.4 Hz, 1H), 3.96 – 3.69 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 204.3, 160.9, 147.3, 147.2, 132.5, 126.9, 121.4, 121.2, 118.2, 118.1, 112.0, 111.9, 111.5, 110.6, 110.1, 109.7, 66.1, 61.9, 55.5. (Method A) conversion 85%, (method B) conversion 95%; (method A) isolated yield = 269 mg, 83%, (method B) isolated yield = 298 mg, 92%.

***(1E,2Z,4E)*-5-((2-Fluorophenyl)amino)-1-((2-fluorophenyl)iminio)penta-2,4-dien-2-olate (3c)**

A capped vial equipped with a magnetic stirrer, furfural (1 mmol), 2-fluoroanaline (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture (A) was stirred at room temperature for 40 minutes (B) underwent microwave irradiation at 60◦C for 10 mins. In each case, the (cooled for method B) reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solutions by methods A and B were concentrated under reduced pressure and the residues were purified by column chromatography (5% ethyl acetate in 95% hexane), according to the previously reported procedure.[38] The product by each method was obtained as red oil, which solidified on standing. Method A provided the sample whose purity is documented by NMR. ^{1}H NMR (500 MHz, DMSO-*d6*) δ 8.35 (s, 1H), 7.61 (dt, *J*= 6.1, 1.7 Hz, 2H), 7.29 – 7.17 (m, 2H), 7.07 (d, *J* = 7.8 Hz, 1H), 7.02 – 6.94 (m, 4H),6.89 – 6.69 (m, 22H), 6.55 (dt, *J* = 3.5, 1.7 Hz, 1H), 6.41 (dt, *J* = 6.1, 1.4 Hz, 1H),3.96 – 3.69 (m, 27H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 204.0, 150.5 (d, $^{1}J_{F,C}$= 238.8 Hz), 150.8 (d, $^{1}J_{F,C}$= 239.9 Hz), 134.9 (d, $^{2}J_{F,C}$= 11.74 Hz), 134.4 (d, $^{2}J_{F,C}$= 11.74 Hz), 123.5 (d, $^{4}J_{F,C}$= 3.39 Hz), 123.3 (d, $^{4}J_{F,C}$= 3.49 Hz), 116.4 (d, $^{3}J_{F,C}$= 6.87 Hz), 116.3 (d, $^{3}J_{F,C}$= 7.03 Hz), 116.2 (d, $^{3}J_{F,C}$= 6.75 Hz), 116.1 (d, $^{3}J_{F,C}$= 7.03 Hz), 113.4 (d, $^{2}J_{F,C}$= 18.83 Hz), 113.2 (d, $^{2}J_{F,C}$= 18.73 Hz), 112.4 (d, $^{4}J_{F,C}$= 3.00 Hz), 112.2 (d, $^{4}J_{F,C}$= 2.47 Hz), 64.6, 59.4. (Method A) conversion 91%, (method B) conversion 94%; (method A) isolated yield = 267 mg, 89% (method B) isolated yield = 276 mg, 92%.

(1E,2Z,4E)-5-((2-(Trifluoromethyl)phenyl)amino)-1-((2-(trifluoromethyl)phenyl)iminio)penta-2,4-dien-2-olate (3d)

Capped vial equipped with a magnetic stirrer, furfural (1 mmol), 2(trifluoromethyl)- aniline (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture (method A) was stirred at room temperature for 40 minutes (method B) underwent microwave irradiation at 60◦C for 10 mins. In each case, the reaction mixture was diluted with DCM (20 mL) and filtered

through Celite. The resultant solutions by methods A and B were concentrated under reduced pressure and the residues were purified by column chromatography (20% ethyl acetate in 80% hexane), according to the previously reported procedure.[38] The product by each method was obtained as red oil, which solidified on standing. Method A provided the sample whose purity is documented by NMR. ^{1}H NMR (500 MHz, DMSO-*d6*) δ 8.19 (s, 1H), 8.01 – 7.95 (m, 1H), 7.75 – 7.44 (m, 17H), 7.36 – 7.29 (m, 5H), 7.25 (d, *J* = 5.1 Hz, 1H), 7.12 (s, 1H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.94 – 6.84 (m, 8H), 6.73 (d, *J* = 8.7 Hz, 1H), 6.64 – 6.57 (m, 5H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-*d6*) δ δ. 151.9, 150.6, 150.5, 147.6, 146.6 (q, $^{4}J_{F,C}$ = 1.7 Hz), 134.2, 133.4, 126.4 (q, $^{3}J_{F,C}$= 5.3 Hz),126.2 (q, $^{3}J_{F,C}$= 5.3 Hz), 125.9, 126.2 (q, $^{1}J_{F,C}$= 273.2 Hz), 124.4 (q, $^{1}J_{F,C}$= 273.6 Hz), 122.4 (q, $^{2}J_{F,C}$= 29.2 Hz), 120.3, 119.1, 117.2, 115.6, 113.1, 111.1 (q, $^{2}J_{F,C}$= 29.2 Hz). (method A) conversion 69%, (method B) conversion 88%, (method A) isolated yield=66% (method B) isolated yield=80%.

***(4S,5R)*-2-bromo-4,5-dimorpholinocyclopent-2-enone (4a)**

Capped vial equipped with a magnetic stirrer, MeCN (dry, 100mL), 3-bromo-2-furaldehyde (1 mmol), morpholine (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture underwent microwave irradiation at 60◦C for 10 mins. The reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solution was concentrated under reduced pressure and the residue purified by column chromatography (60% ethyl acetate in 40% hexane). The product was obtained as yellow oil. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 2.4 Hz, 1H), 3.76 – 3.63 (m, 9H), 3.38 (d, *J* = 2.9 Hz, 1H), 2.85 (dt, *J* = 10.2, 4.6 Hz, 2H), 2.62 (tdd, *J* = 17.0, 11.6, 4.5 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 198.3, 158.4, 126.8, 111.5, 110.8, 110, 67.4, 67.2, 67.0, 66.3, 60.35, 50.1, 49.8. HRMS (ESI-FTMS) *m/z*: ([M + H]$^{+}$)

calcd for $C_{13}H_{20}Br_1N_2O_3$ 331.0657; found 331.0647. Conversion 93%; isolated yield = 303 mg, 92%.

(4S,5R)-2-bromo-4,5-bis(diallylamino)cyclopent-2-enone (4b)

Capped vial equipped with a magnetic stirrer, MeCN (dry, 100mL), 3-bromo-2-furaldehyde (1 mmol), diallylamine (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture underwent microwave irradiation at 60◦C for 10 mins. The reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solution was concentrated under reduced pressure and the residue purified by column chromatography (5% ethyl acetate in 95% hexane). The product was obtained as yellow oil. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 2.3 Hz, 1H), 5.81 (dtdd, *J* = 15.8, 10.5, 5.6, 2.9 Hz, 3H), 5.22 (dt, *J* = 17.2, 1.7 Hz, 3H), 5.17 – 5.10 (m, 3H), 4.04 (t, *J* = 2.8 Hz, 1H), 3.68 (d, *J* = 3.1 Hz, 1H), 3.32 (dd, *J* = 14.0, 7.7 Hz, 2H), 3.23 – 3.18 (m, 2H), 3.20 – 3.09 (m, 3H), 1.30 – 1.24 (m, 1H), 1.24 (s, 2H), 0.90 – 0.79 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 200.0, 160.5, 136.1, 135.9, 125.8, 118.0, 117.7, 64.6, 63.4, 54.5, 53.7. HRMS (ESI-FTMS) *m/z*: ([M + H]$^+$) calcd for $C_{17}H_{24}Br_1N_2O_1$ 351.1071, found 351.1067. Conversion>99%; isolated yield = 333 mg, 95%.

(4S,5R)-2-bromo-4,5-di(indolin-1-yl)cyclopent-2-enone (4c)

Capped vial equipped with a magnetic stirrer, MeCN (dry, 100mL), 3-bromo-2-furaldehyde (1 mmol), indoline (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture underwent microwave irradiation at 60◦C for 10 mins. The reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solution was concentrated under reduced pressure and the residue purified by column chromatography (60% ethyl acetate in 40% hexane). The product was obtained as yellow oil. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.79 (d, *J*

= 2.3 Hz, 1H), 7.08 (ddd, *J* = 19.4, 7.3, 1.3 Hz, 2H), 6.99 (td, *J* = 7.7, 1.2 Hz, 1H), 6.93 (td, *J* = 7.8, 1.3 Hz, 1H), 6.68 (dtd, *J* = 27.4, 7.5, 0.9 Hz, 2H), 6.37 (d, *J* = 7.8 Hz, 1H), 6.07 (d, *J* = 7.8 Hz, 1H), 4.95 (dd, *J* = 3.6, 2.4 Hz, 1H), 4.49 (d, *J* = 3.6 Hz, 1H), 3.58 – 3.47 (m, 2H), 3.39 (ddt, *J* = 33.6, 9.7, 8.3 Hz, 2H), 3.03 – 2.98 (m, 4H). $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d_6) δ 195.9, 161.4, 150.8, 150.6, 129.4, 128.9, 127.4, 124.6, 124.4, 117.8, 117.3, 107.5, 106.7, 62.2, 58.2, 53.1, 49.5, 48.4, 40.5, 27.8, 27.7. HRMS (ESI-FTMS) *m/z*: ($[M + Na]^+$) calcd for $C_{21}H_{19}Br_1N_2Na_1O_1$ 417.0578, found 417.0573. Conversion 97%, isolated yield = 370 mg, 94%.

(4S,5R)-2-bromo-4,5-bis(3,4-dihydroisoquinolin-2(1H)-yl)cyclopent-2-enone (4d)

Capped vial equipped with a magnetic stirrer, MeCN (dry, 100mL), 3-bromo-2-furaldehyde (1 mmol), 1,2,3,4- Tetrahydroisoquinoline (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture underwent microwave irradiation at 60◦C for 10 mins. The reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solution was concentrated under reduced pressure and the residue purified by column chromatography (5% ethyl acetate in 95% hexane).^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.82 (s, 1H), 7.17 – 7.07 (m, 6H), 7.03 – 6.97 (m, 2H), 4.21 (d, *J* = 14.6 Hz, 1H), 4.08 (s, 1H), 3.94 – 3.85 (m, 3H), 3.71 (d, *J* = 2.9 Hz, 1H), 3.07 (dt, *J* = 12.1, 5.6 Hz, 1H), 2.90 (dq, *J* = 17.1, 6.6, 5.5 Hz, 7H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-*d*) δ 199.2, 159.3, 134.6, 134.2, 134.0, 133.9, 128.8, 126.7, 126.6, 126.4, 126.4, 126.1, 125.8, 125.6, 67.1, 66.7, 60.4, 52.7, 52.1, 47.3, 47.2, 29.9, 29.4. The product was obtained as yellow oil. HRMS (ESI-FTMS) *m/z*: ($[M + H]^+$) calcd for $C_{23}H_{24}Br_1N_2O_1$ 423.1071, found 423.1068. Conversion 50%, isolated yield = 202 mg, 48%.

(1E,2E,4E)-3-bromo-5-(phenylamino)-1-(phenyliminio)penta-2,4-dien-2-olate (5a)

Capped vial equipped with a magnetic stirrer, MeCN (dry, 100mL), 3-bromo-2-furaldehyde (1 mmol), aniline (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture underwent microwave irradiation at 60◦C for 10 mins. The reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solution was concentrated under reduced pressure and the residue purified by column chromatography (5% ethyl acetate in 95% hexane).The product was obtained as yellow oil. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.95 (d, J = 2.1 Hz, 1H), 7.08 – 7.05 (m, 2H), 7.04 – 7.01 (m, 2H), 6.66 – 6.63 (m, 2H), 6.59 – 6.52 (m, 4H), 6.22 (s, 2H), 4.61 (s, 1H), 4.19 (d, J = 3.2 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 198.5, 160.2, 147.8, 147.4, 124.1, 117.40, 117.0, 113.2, 112.9, 63.4, 59.0, 39.9. HRMS (ESI-FTMS) *m/z*: ([M - H]$^-$) calcd for $C_{17}H_{14}Br_1N_2O$ 341.0289, found 341.0292. Conversion 98%, isolated yield = 398 mg, 96%.

(1E,2E,4E)-3-bromo-5-((2-fluorophenyl)amino)-1-((2-fluorophenyl)iminio)penta-2,4-dien-2-olate (5b)

Capped vial equipped with a magnetic stirrer, MeCN (dry, 100mL), 3-bromo-2-furaldehyde (1 mmol), 2-Fluoroaniline (2.2 mmol) and 3 mg of catalyst (0.01% total of Dy) were added. The resultant mixture underwent microwave irradiation at 60◦C for 10 mins. The reaction mixture was diluted with DCM (20 mL) and filtered through Celite. The resultant solution was concentrated under reduced pressure and the residue purified by column chromatography (5% ethyl acetate in 95% hexane). The product was obtained as yellow oil. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.96 (d, J = 2.1 Hz, 1H), 7.05 – 6.81 (m, 5H), 6.77 – 6.67 (m, 1H), 6.56 (dtdd, J = 21.6, 7.8, 4.8, 1.6 Hz, 2H), 6.11 (dd, J = 9.5, 2.2 Hz, 1H), 6.04 (dd, J = 9.3, 2.4 Hz, 1H), 4.83 – 4.77 (m, 1H), 4.54 (dd, J = 9.2, 3.5 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 197.6, 159.5, 151.0 (d, $^{1}J_{F,C}$= 237.6 Hz), 150.7 (d, $^{1}J_{F,C}$= 237.4 Hz), 135.6 (d, $^{2}J_{F,C}$= 11.2 Hz), 135.1 (d, $^{2}J_{F,C}$= 11.5 Hz),124.9 (d, $^{4}J_{F,C}$=

3.7 Hz), 124.6 (d, $^{4}J_{F,C}$= 3.3 Hz), 123.9, 116.8 (d, $^{3}J_{F,C}$= 7.2 Hz), 116.5 (d, $^{3}J_{F,C}$= 7.4 Hz), 114.7 (d, $^{2}J_{F,C}$= 18.2 Hz), 114.6 (d, $^{2}J_{F,C}$= 18.2 Hz), 112.6 (d, $^{3}J_{F,C}$= 3.4 Hz), 112.5 (d, $^{3}J_{F,C}$= 3.6 Hz), 62.9, 58.8. HRMS (ESI-FTMS) *m/z*: ([M - H]$^{+}$) calcd for $C_{17}H_{12}Br_1F_2N_2O$ 377.0101, found 377.0098. Conversion 89%, isolated yield = 329 mg, 87%.

Acknowledgement

GEK acknowledges the EPSRC (UK) for funding (grant number EP/ M023834/1). AM thanks Wellcome (ISSF) and Niemann Pick Research Foundation for funding. We thank the EPSRC UK National Crystallography Service at the University of Southampton for the collection of the crystallographic data for **3a HCl**. [56]

The Supporting Information is available free of charge on the ACS Publications website at DOI:10.1021/acs.joc.7b03051. CCDC 1891851 and 1891852 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge viawww.ccdc.cam.ac.uk/data_request/cif, or by email in data_request@ccdc.cam.ac.uk or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: + 44 1223 336033. Copies of ^{1}H, ^{13}C-NMR and HRMS spectra of the products, copies of IR, UV-Vis, TGA and ESI-MS of the catalyst **1**, X-ray data for **1** (CIF) and **3aHCl** (CIF) and xyz coordinates for **3a, 3aTS** and **Stenhouse salt.**

References

(1) Rösler, S.; Ertl, M.; Irrgang, T.; Kempe, R. Cobalt-Catalyzed Alkylation of Aromatic Amines by Alcohols. *Angew. Chem. Int. Ed.* **2015**, *54*, 15046–15050.

(2) Kallmeier, F.; Dudziec, B.; Irrgang, T.; Kempe, R. Manganese-Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols. *Angew. Chem. Int. Ed.* **2017**, *56*,

7261–7265.
(3) Maayan, G.; Gluz, N.; Christou, G. A Bioinspired Soluble Manganese Cluster as a Water Oxidation Electrocatalyst with Low Overpotential. *Nat. Catal.* **2018**, *1*, 48–54.
(4) Okamura, M.; Kondo, M.; Kuga, R.; Kurashige, Y.; Yanai, T.; Hayami, S.; Praneeth, V. K. K.; Yoshida, M.; Yoneda, K.; Kawata, S.; et al. A Pentanuclear Iron Catalyst Designed for Water Oxidation. *Nature* **2016**, *530*, 465–468.
(5) Song, F.; Moré, R.; Schilling, M.; Smolentsev, G.; Azzaroli, N.; Fox, T.; Luber, S.; Patzke, G. R. {Co4O4} and {CoxNi4-XO4} Cubane Water Oxidation Catalysts as Surface Cut-Outs of Cobalt Oxides. *J. Am. Chem. Soc.* **2017**, *139*, 14198–14208.
(6) Yu, J.; Jiang, H. J.; Zhou, Y.; Luo, S. W.; Gong, L. Z. Sodium Salts of Anionic Chiral Cobalt(III) Complexes as Catalysts of the Enantioselective Povarov Reaction. *Angew. Chem. Int. Ed.* **2015**, *54*, 11209–11213.
(7) Lange, J. P.; Van Der Heide, E.; Van Buijtenen, J.; Price, R. Furfural-A Promising Platform for Lignocellulosic Biofuels. *ChemSusChem* **2012**, *5*, 150–166.
(8) Mittal, A.; Black, S. K.; Vinzant, T. B.; O'Brien, M.; Tucker, M. P.; Johnson, D. K. Production of Furfural from Process-Relevant Biomass-Derived Pentoses in a Biphasic Reaction System. *ACS Sustain. Chem. Eng.* **2017**, *5*, 5694–5701.
(9) Luo, Y.; Li, Z.; Li, X.; Liu, X.; Fan, J.; Clark, J. H.; Hu, C. The Production of Furfural Directly from Hemicellulose in Lignocellulosic Biomass: A Review. *Catal. Today* **2019**, *319*, 14–24.
(10) Cui, X.; Zhao, X.; Liu, D. A Novel Route for the Flexible Preparation of Hydrocarbon Jet Fuels from Biomass-Based Platform Chemicals: A Case of Using Furfural and 2,3-Butanediol as Feedstocks. *Green Chem.* **2018**, *20*, 2018–2026.
(11) Di Gioia, M. L.; Nardi, M.; Costanzo, P.; De Nino, A.; Maiuolo, L.; Oliverio, M.; Procopio, A. Biorenewable Deep Eutectic Solvent for Selective and Scalable Conversion of Furfural into Cyclopentenone Derivatives. *Molecules* **2018**, *23*, 1891.
(12) Matsunaga, S.; Shibasaki, M. Recent Advances in Cooperative Bimetallic Asymmetric Catalysis: Dinuclear Schiff Base Complexes. *Chem. Commun.* **2014**, *50*, 1044–1057.
(13) Park, J.; Hong, S. Cooperative Bimetallic Catalysis in Asymmetric Transformations. *Chem. Soc. Rev.* **2012**, *41*, 6931–6943.
(14) Mankad, N. P. Selectivity Effects in Bimetallic Catalysis. *Chem. Eur. J.* **2016**, *22*, 5822–5829.
(15) Handa, S.; Nagawa, K.; Sohtome, Y.; Matsunaga, S.; Shibasaki, M. A Heterobimetallic Pd/La/Schiff Base Complex for Anti-Selective Catalytic Asymmetric Nitroaldol Reactions and Applications to Short Syntheses of β-Adrenoceptor Agonists. *Angew. Chem. Int. Ed.* **2008**, *47*, 3230–3233.
(16) Furutachi, M.; Mouri, S.; Matsunaga, S.; Shibasaki, M. A Heterobimetallic Ni/La-Salan Complex for Catalytic Asymmetric Decarboxylative 1,4-Addition of Malonic Acid Half-Thioester. *Chem. Asian J.* **2010**, *5*, 2351–2354.
(17) Pye, D. R.; Mankad, N. P. Bimetallic Catalysis for C–C and C–X Coupling Reactions. *Chem. Sci.* **2017**, *8*, 1705–1718.
(18) Griffiths, K.; Tsipis, A. C.; Kumar, P.; Townrow, O. P. E.; Abdul-Sada, A.; Akien, G. R.; Baldansuren, A.; Spivey, A. C.; Kostakis, G. E. 3d/4f Coordination Clusters as Cooperative Catalysts for Highly Diastereoselective Michael Addition Reactions. *Inorg. Chem.* **2017**, *56*, 9563–9573.
(19) Kumar, P.; Griffiths, K.; Lymperopoulou, S.; Kostakis, G. E. Tetranuclear Zn_2Ln_2

Coordination Clusters as Catalysts in the Petasis Borono-Mannich Multicomponent Reaction. *RSC Adv.* **2016**, *6*, 79180–79184.
(20) Kumar, P.; Lymperopoulou, S.; Griffiths, K.; Sampani, S.; Kostakis, G. E. Highly Efficient Tetranuclear ZnII2LnIII2 Catalysts for the Friedel–Crafts Alkylation of Indoles and Nitrostyrenes. *Catalysts* **2016**, *6*, 140.
(21) Griffiths, K.; Kumar, P.; Akien, G. R.; Chilton, N. F.; Abdul-Sada, A.; Tizzard, G. J.; Coles, S. J.; Kostakis, G. E. Tetranuclear Zn/4f Coordination Clusters as Highly Efficient Catalysts for Friedel–Crafts Alkylation. *Chem. Commun.* **2016**, *52*, 7866–7869.
(22) Kumar, P.; Griffiths, K.; Anson, C.; Powell, A. K.; Kostakis, G. E. Tetranuclear CuII2DyIII2 Coordination Cluster as Suzuki (C–C) Coupling Reaction Promoter. *Dalton Trans.* **2018**, *47*, 17202–17205.
(23) Veits, G. K.; Read de Alaniz, J. Dysprosium(III) Catalysis in Organic Synthesis. *Tetrahedron* **2012**, *68*, 2015–2026.
(24) Nguyen, A. I.; Wang, J.; Levine, D. S.; Ziegler, M. S.; Tilley, T. D. Synthetic Control and Empirical Prediction of Redox Potentials for Co 4 O 4 Cubanes over a 1.4 V Range: Implications for Catalyst Design and Evaluation of High-Valent Intermediates in Water Oxidation. *Chem. Sci.* **2017**, *8*, 4274–4284.
(25) Clatworthy, E. B.; Li, X.; Masters, A. F.; Maschmeyer, T. Electrochemical Investigation of [Co 4 (μ 3 -O) 4 (μ-OAc) 4 (Py) 4] and Peroxides by Cyclic Voltammetry. *Chem. Commun.* **2016**, *52*, 14412–14415.
(26) Reymond, S.; Cossy, J. Copper-Catalyzed Diels - Alder Reactions. *Chem. Rev.* **2008**, *108*, 5359–5406.
(27) Li, S.-W.; Batey, R. A. Mild Lanthanide(III) Catalyzed Formation of 4,5-Diaminocyclopent-2-Enones from 2-Furaldehyde and Secondary Amines: A Domino Condensation/Ring-Opening/Electrocyclization Process. *Chem. Commun.* **2007**, 3759–3761.
(28) Verrier, C.; Moebs-Sanchez, S.; Queneau, Y.; Popowycz, F. The Piancatelli Reaction and Its Variants: Recent Applications to High Added-Value Chemicals and Biomass Valorization. *Org. Biomol. Chem.* **2018**, *16*, 676–687.
(29) Nayani, K.; Cinsani, R.; Hussaini SD, A.; Mainkar, P. S.; Chandrasekhar, S. Brønsted Acid Catalyzed Domino Aza-Piancatelli Rearrangement/Michael Reaction: Construction of 1,4-Benzodiazepin-5-Ones in One Pot. *Eur. J. Org. Chem.* **2017**, *2017*, 5671–5678.
(30) Palmer, L. I.; de Alaniz, J. R. Direct and Highly Diastereoselective Synthesis of Azaspirocycles by a Dysprosium(III) Triflate Catalyzed Aza-Piancatelli Rearrangement. *Angew. Chem. Int. Ed.* **2011**, *50*, 7167–7170.
(31) Veits, G. K.; Wenz, D. R.; Read de Alaniz, J. Versatile Method for the Synthesis of 4-Aminocyclopentenones: Dysprosium(III) Triflate Catalyzed Aza-Piancatelli Rearrangement. *Angew. Chem. Int. Ed.* **2010**, *49*, 9484–9487.
(32) Gomes, R. F. A.; Coelho, J. A. S.; Afonso, C. A. M. Synthesis and Applications of Stenhouse Salts and Derivatives. *Chem. - A Eur. J.* **2018**, *24*, 9170–9186.
(33) Gomes, R. F. A.; Esteves, N. R.; Coelho, J. A. S.; Afonso, C. A. M. Copper(II) Triflate As a Reusable Catalyst for the Synthesis of Trans -4,5-Diamino-Cyclopent-2-Enones in Water. *J. Org. Chem.* **2018**, *83*, 7509–7513.
(34) Procopio, A.; Costanzo, P.; Curini, M.; Nardi, M.; Oliverio, M.; Sindona, G. Erbium(III) Chloride in Ethyl Lactate as a Smart Ecofriendly System for Efficient and Rapid Stereoselective Synthesis of Trans-4,5-Diaminocyclopent-2- Enones. *ACS Sustain. Chem.*

Eng. **2013**, *1*, 541–544.
(35) Nardi, M.; Costanzo, P.; De Nino, A.; Di Gioia, M. L.; Olivito, F.; Sindona, G.; Procopio, A. Water Excellent Solvent for the Synthesis of Bifunctionalized Cyclopentenones from Furfural. *Green Chem.* **2017**, *19*, 5403–5411.
(36) Nunes, J. P. M.; Afonso, C. A. M.; Caddick, S. Synthesis of 2,4-Bifunctionalised Cyclopentenones from 2-Furaldehyde. *RSC Adv.* **2013**, *3*, 14975–14978.
(37) Estevão, M. S.; Afonso, C. A. M. Synthesis of Trans-4,5-Diaminocyclopent-2-Enones from Furfural Catalyzed by Er(III) Immobilized on Silica. *Tetrahedron Lett.* **2017**, *58*, 302–304.
(38) Griffiths, K.; Kumar, P.; Mattock, J. D.; Abdul-Sada, A.; Pitak, M. B.; Coles, S. J.; Navarro, O.; Vargas, A.; Kostakis, G. E. Efficient NiII2LnIII2 Electrocyclization Catalysts for the Synthesis of Trans-4,5-Diaminocyclopent-2-Enones from 2-Furaldehyde and Primary or Secondary Amines. *Inorg. Chem.* **2016**, *55*, 6988–6994.
(39) Griffiths, K.; Gallop, C. W. D.; Abdul-Sada, A.; Vargas, A.; Navarro, O.; Kostakis, G. E. Heteronuclear 3 d/DyIII Coordination Clusters as Catalysts in a Domino Reaction. *Chem. Eur. J.* **2015**, *21*, 6358–6361.
(40) Lewis, K. G.; Mulquiney, C. E. Aspects of the Formation and Use of Stenhouse Salts and Related Compounds. *Tetrahedron* **1977**, *33*, 463–475.
(41) Stenhouse, J. Linked Supramolecular Building Blocks for Enhanced Cluster Formation. *Justus Liebigs Ann. Chem.* **1850**, *74*, 278–279.
(42) Marin, L.; Gandon, V.; Schulz, E.; Lebœuf, D. One-Pot Assembly of Highly Functionalized Cyclopenta[b]Pyrroles via a Calcium(II)- and Copper(II)-Catalyzed Reaction Sequence. *Adv. Synth. Catal.* **2017**, *359*, 1157–1163.
(43) Dhakal, B.; Bohé, L.; Crich, D. Trifluoromethanesulfonate Anion as Nucleophile in Organic Chemistry. *J. Org. Chem.* **2017**, *82*, 9263–9269.
(44) Prat, D.; Hayler, J.; Wells, A. A Survey of Solvent Selection Guides. *Green Chem.* **2014**, *16*, 4546–4551.
(45) Ramesh, D.; Reddy, T. S.; Narasimhulu, M.; Rajaram, S.; Suryakiran, N.; Mahesh, K. C.; Venkateswarlu, Y. Efficient and Rapid Stereoselective Synthesis of Trans-4,5-Diaminocyclopent-2-Enones by Acidic Ionic Liquid under Solvent-Free Conditions. *Chem. Lett.* **2009**, *38*, 586–587.
(46) Spencer, J.; Baltus, C. B.; Patel, H.; Press, N. J.; Callear, S. K.; Male, L.; Coles, S. J. Microwave-Mediated Synthesis of an Arylboronate Library. *ACS Comb. Sci.* **2011**, *13*, 24–31.
(47) Hiscox, A.; Ribeiro, K.; Batey, R. A. Lanthanide(III)-Catalyzed Synthesis of Trans - Diaminocyclopentenones from Substituted Furfurals and Secondary Amines via a Domino Ring-Opening/4π-Electrocyclization Pathway. *Org. Lett.* **2018**, *20*, 6668–6672.
(48) Padayachy, K.; Mgcima, Z.; Fernandes, M. A.; Marques, H. M.; Sousa, A. S. de; IUCr. Hydrogen-Bond Interactions in Morpholinium Bromide. *Acta Crystallogr. Sect. E Struct. Reports Online* **2011**, *67*, o2594–o2594.
(49) Anderson, K. M.; Goeta, A. E.; Hancock, K. S. B.; Steed, J. W. Unusual Variations in the Incidence of $Z' > 1$ in Oxo-Anion Structures. *Chem. Commun.* **2006**, 2138–2140.
(50) Mwenda, E. T.; Nguyen, H. M. Enantioselective Synthesis of 1,2-Diamines Containing Tertiary and Quaternary Centers through Rhodium-Catalyzed DYKAT of Racemic Allylic Trichloroacetimidates. *Org. Lett.* **2017**, *19*, 4814–4817.
(51) Das, S.; Daniliuc, C. G.; Studer, A. Stereospecific 1,3-Aminobromination of Donor–Acceptor Cyclopropanes. *Angew. Chemie - Int. Ed.* **2017**, *56*, 11554–11558.

(52) Singh, G.; Arora, A.; Rani, S.; Kalra, P.; Aulakh, D.; Wriedt, M. A Family of Silatrane-Armed Triazole-Encapped Salicylaldehyde-Derived Schiff Bases: Synthesis, Spectral Analysis, and Antimicrobial and Quantum Chemical Evaluation. *Appl. Organomet. Chem.* **2017**, *31*, e3728.
(53) Raj, P.; Singh, A.; Singh, A.; Singh, N. Syntheses and Photophysical Properties of Schiff Base Ni(II) Complexes: Application for Sustainable Antibacterial Activity and Cytotoxicity. *ACS Sustain. Chem. Eng.* **2017**, *5*, 6070–6080.
(54) Allen, F. H. The Cambridge Structural Database: A Quarter of a Million Crystal Structures and Rising. *Acta Crystallogr. Sect. B-Structural Sci.* **2002**, *58*, 380–388.
(55) Yu, D.; Thai, V. T.; Palmer, L. I.; Veits, G. K.; Cook, J. E.; Read De Alaniz, J.; Hein, J. E. Importance of Off-Cycle Species in the Acid-Catalyzed Aza-Piancatelli Rearrangement. *J. Org. Chem.* **2013**, *78*, 12784–12789.
(56) Coles, S. J.; Gale, P. A. Changing and Challenging Times for Service Crystallography. *Chem. Sci.* **2012**, *3*, 683–689.

Table of Contents