Electronic Supplementary Material (ESI) for Green Chemistry

Direct amide bond formation from carboxylic acids and amines using activated alumina balls as a new, convenient, clean, reusable and low cost heterogeneous catalyst

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Supplementary Information
Part 1

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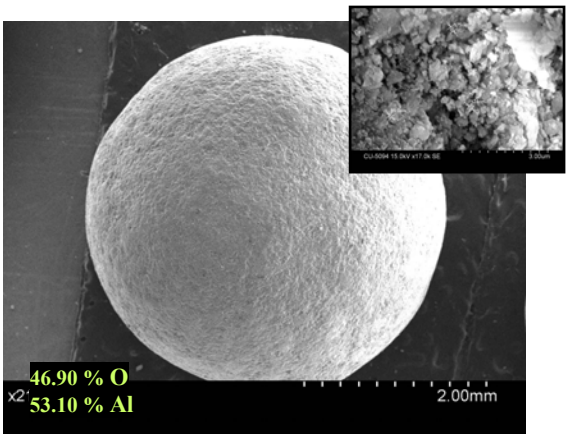


Figure S1 SEM image of the whole alumina ball; Inset: close-up SEM image of the alumina ball before calcination. The SEM images of an activated alumina ball show aggregates of particles and the highly porous nature of the catalyst (inset). The self-aggregated particle size before calcination is 99-175 nm (evident by enlargement of the inset SEM image).

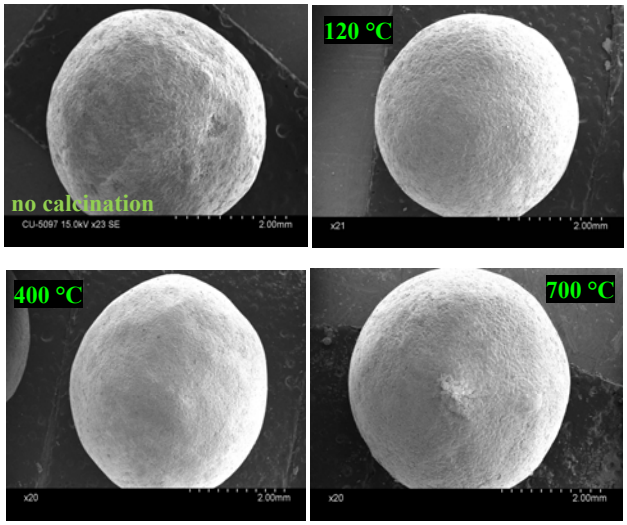


Figure S2 Clockwise from top left: The SEM images of an activated alumina ball before calcination and after calcination at 120 °C, 400 °C and 700 °C. There is no visible change of the alumina ball to the naked eye, but the close-up high resolution SEM images show that significant morphological changes have occurred on calcinations to 120 °C, 400 °C and 700 °C (given below).

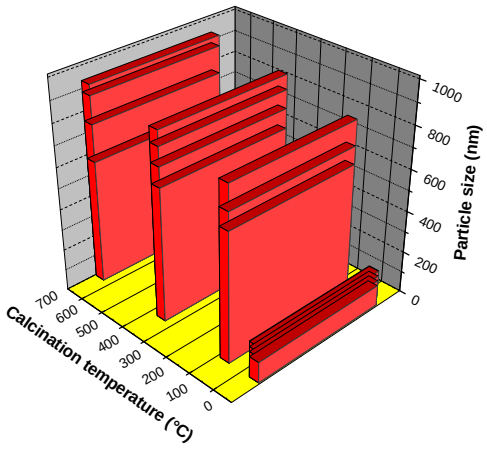


Figure S3 Change in particle size aggregates with increase in calcination temperature of the activated alumina ball catalyst.

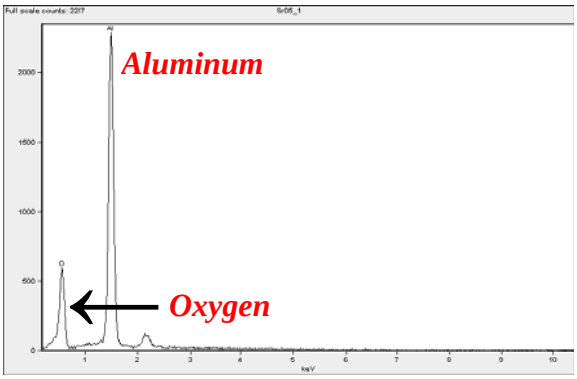


Figure S4 EDS X-ray spectrum of an activated alumina ball.

Table S1 Quantitative results of the EDS X-ray spectrum of an activated alumina ball.

Element	Net Counts	Weight %	Weight % Error	Atom %	Atom % Error
O	5581	46.90	+/- 0.79	59.84	+/- 1.01
Al	24935	53.10	+/- 0.40	40.16	+/- 0.30
Total		100.00		100.00	

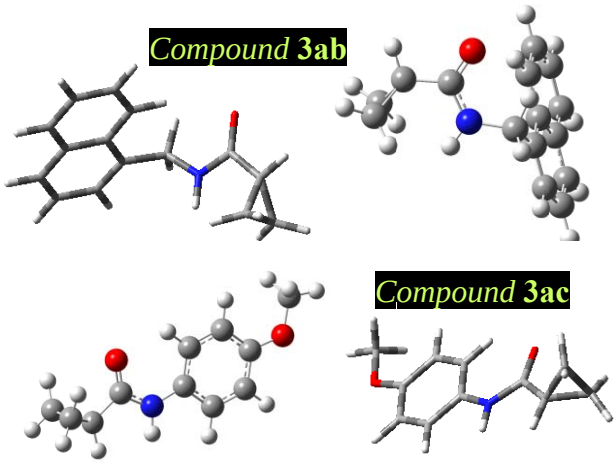


Figure S5 Different views of the DFT optimised structure of compound **3ab** and **3ac** showing the non-equivalent chemical environment for the methylene protons in the cyclopropyl ring. It is interesting to note that the methylene protons for the cyclopropyl ring (compounds **3ab** and **3ac**) give two distinct ^{1}H NMR signals, indicating they have become chemically non-equivalent (Figure 7 and Figure 8). As can be seen from the DFT optimised structures below, both the cyclopropyl-C*H*$_2$'s are directed *away* from the amide carbonyl in case of compound **3ab** and *towards* the amide carbonyl in case of compound **3ac**. Again, out of the two protons in a cyclopropyl-C*H*$_2$, one proton is above the cyclopropyl plane and another below this plane with respect to the amide carbonyl (as designated by the wedge bonds, Figure 8). These methylene protons thus become chemically non-equivalent. Due to the diamagnetic anisotropic effect of the carbonyl group, one proton each from the two cyclopropyl - C*H*$_2$'s falls in the paramagnetic deshielding zone. This effect is very prominent in **3ac** where there is a downfield cyclopropyl-methylene CH*H* signal at δ 1.01 for two similar adjacent protons. Likewise, the other two similar adjacent protons appear upfield at δ (0.77-0.72) (Figure S6).

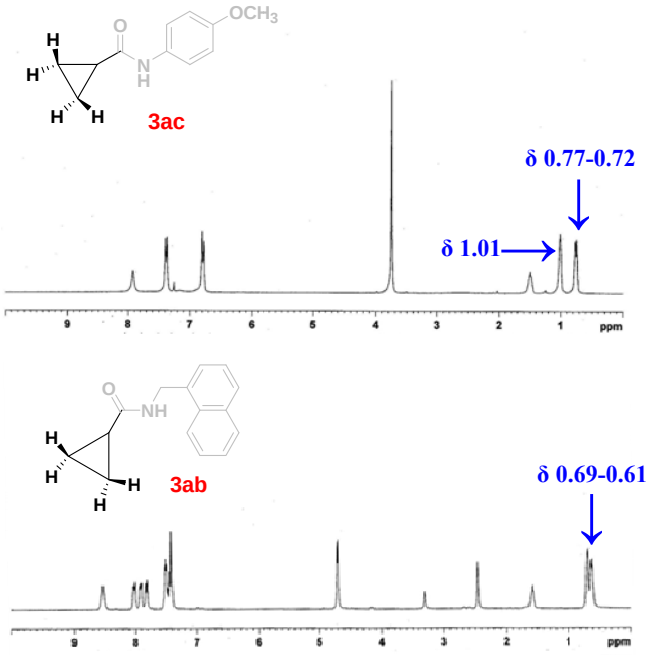
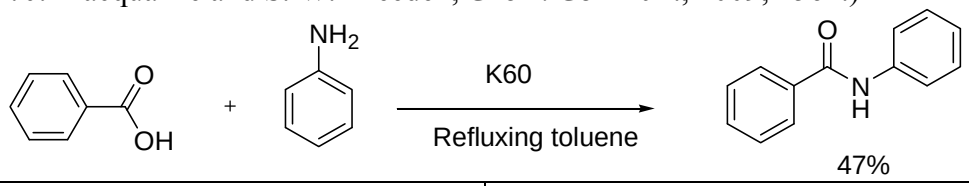


Figure S6 ^{1}H NMR of compounds **3ac** (above) and **3ab** (below) depicting the splitting of the cyclopropyl-C*H*$_2$ signals. The two adjacent CH*H* signals for **3ac** are at δ 1.01 and δ (0.77-0.72). Due to diamagnetic anisotropic effect of the amide carbonyl group, one proton each from the cyclopropyl C*H*$_2$'s fall in the paramagnetic deshielding zone. For compound **3ab**, the cyclopropyl-C*H*$_2$'s are more chemically equivalent than **3ac** and therefore come close together rather than two sets of signals wide apart at δ (0.69-0.61).

Calculations for the synthesis of *N*-Phenyl-benzamide using K60 silica gel (J. W. Comerford, J. H. Clark, D. J. Macquarrie and S. W. Breeden, *Chem. Commun*., 2009, 2562.)



47%

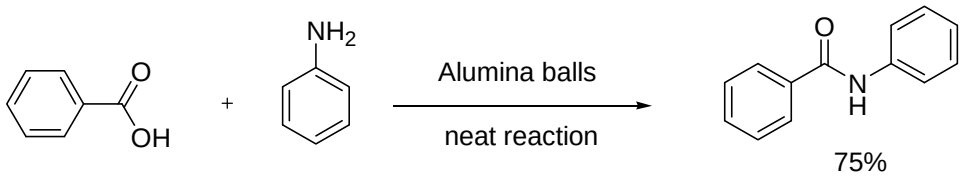
Input		Output	
Benzoic acid	1.47g (12mmols)	*N*-Phenyl-benzamide	1.11g
Aniline	1.12g (12mmols)	Organic solvent waste (90% recovery)	1.73g
Toluene	17.34g (20ml)	K60 catalyst	1.30g
K60	1.30g (50% wt)	Total waste	3.03g
Total	21.23g		

E-Factor
(3.03g waste/ 1.11g of product) = 2.73

Mass intensity
(21.23g of raw materials used/1.11g of crude product) = 19.13 (much away from ideal result)

Atom economy
[197/ (122+ 93)]×100% = 92%

Calculations for the synthesis of *N*-Phenyl-benzamide using activated alumina balls (our methodology)



75%

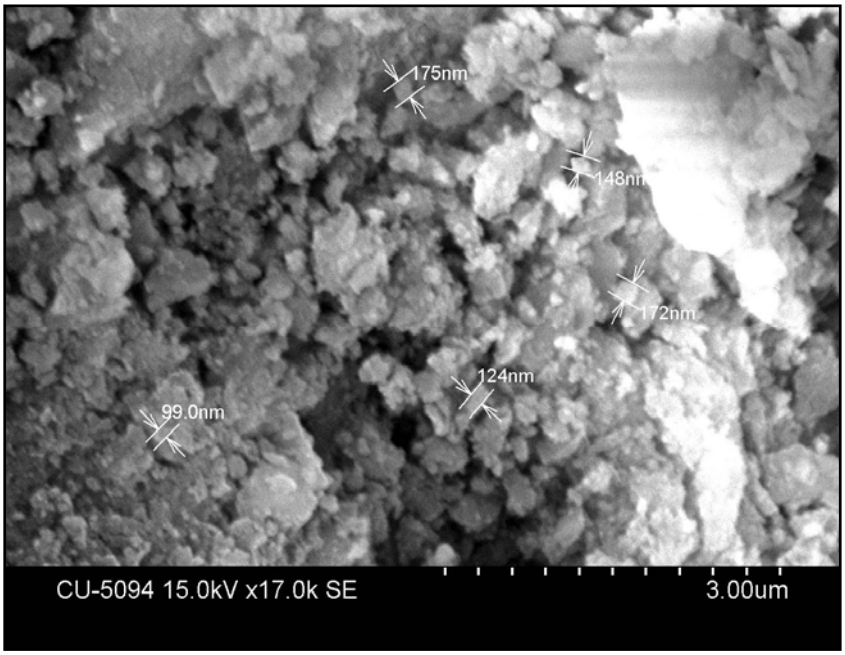
Input		Output	
Benzoic acid	1.22g (10mmols)	*N*-Phenyl-benzamide	1.48g
Aniline	0.93g (10mmols)	Alumina ball catalyst	0.22g
Alumina ball catalyst	0.22g (10% wt)	Total waste	0.22g
Total	2.37g		

E-Factor
(0.22g waste/ 1.48g of product) = 0.15

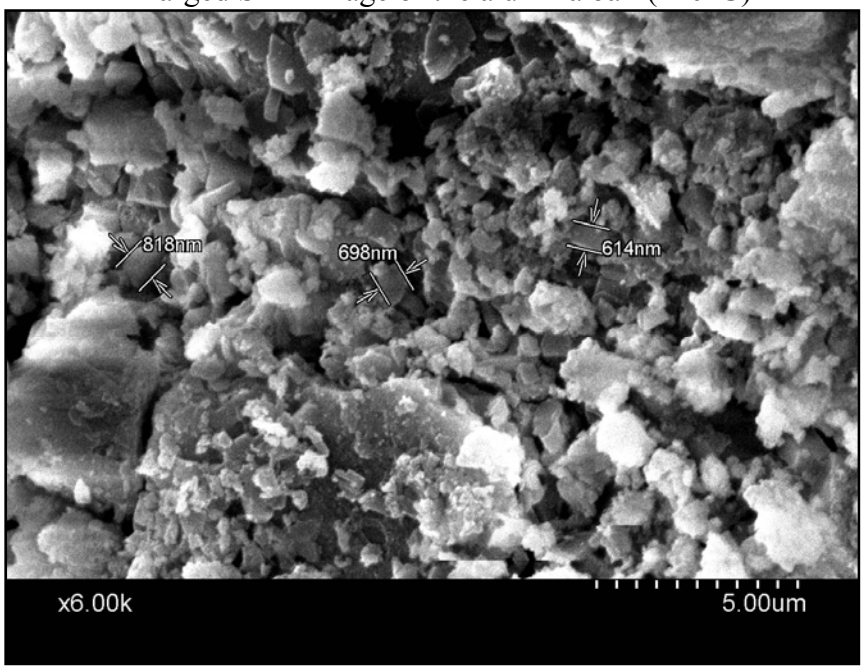
Mass intensity
(2.37g of raw materials used/1.48g of crude product) = 1.60 (almost towards ideal result)

Atom economy
[197/ (122+ 93)]×100% = 92%

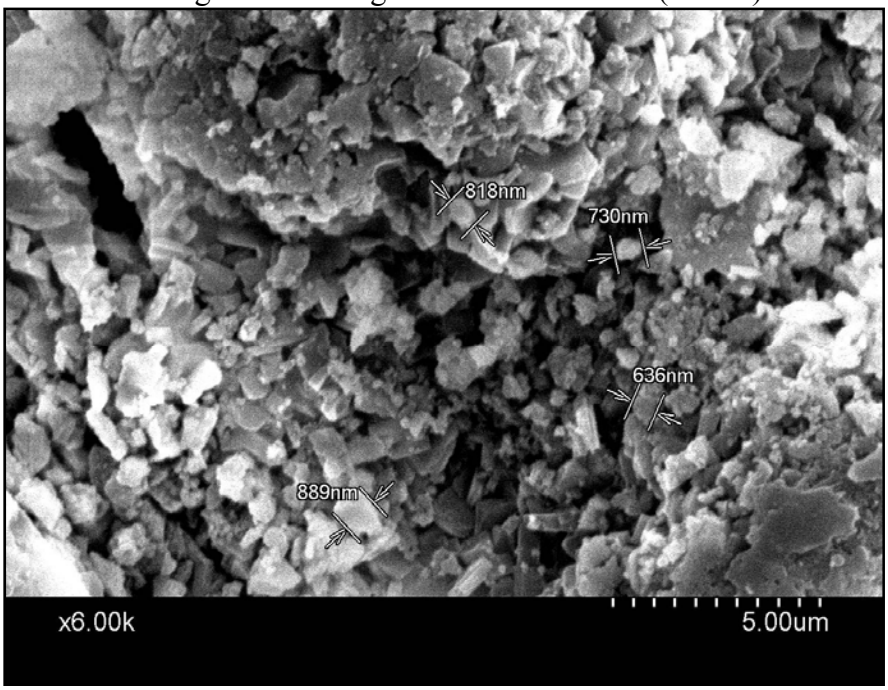
Enlarged SEM image of the alumina ball (**no calcination**)



Enlarged SEM image of the alumina ball (**120°C**)



Enlarged SEM image of the alumina ball (**400°C**)



Enlarged SEM image of the alumina ball (**700°C**)