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Microwave-Assisted Green Catalytic Techniques: A Phosphine-Free Heck Reactive, One-Pot Amide Formation, And A Sustainable Preparation Of 2h-Indazoles [2,1-B] Phthalazinetriones

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Abstract

In many fields, including industry, engineering, and medicine, amides play a crucial role as synthetic raw materials. An elegant functional embellishment with well-heeled chemistry, the amide group is present in a wide variety of bioactive compounds. An appealing field has been the development of sustainable and efficient technologies for amide synthesis. Since synthetic chemists are now interested in transition metal-mediated organic transformations, this study aims to identify transition metal catalysts that may have industrial and environmental applications. This paper offers a detailed exploration of the development of the green and efficient catalytic systems based on the forming of the carbon–carbon and carbon–nitrogen bonds by using the carbon-carbon and carbon-nitrogen transition-metal-mediated catalytic techniques. An unprecedented phosphine-free palladium complex, Pd[(L)-Proline] 2 was prepared and used as a recyclable and water-soluble catalyst in Heck coupling reactions under aqueous conditions with the assistance of microwave. The identical environmentally friendly methodology was applied in the preparation of the primary amides by the one-pot reaction of aldehydes with hydroxylamine hydrochloride catalyzed by Sc $(OTf)_3$ and also to the preparation of the 2H-indazolo[2,1-b] phthalazinetrione derivatives by the use of $KHSO_4$ SiO_2 as a solid acid catalyst in solvent-free conditions. All the reactions were carried out at low intensity of the microwave irradiation with high yields (78-95) and short reaction times (10-50 min). The catalyst was very air and moisture stable and its application in solvent (water) complies with the concepts of green chemistry. IR, ^{1}H NMR, and ^{13}C NMR spectroscopy were used to confirm that the synthesized products were structurally explained.

Keywords: Catalytic, Microwave-Assisted, One-Pot Amide, 2h-Indazoles [2,1-B] etc.

Introduction

One rapidly realizes that carbon-carbon bond-forming reactions are the most influential kind of reaction when tracing the history of organic chemistry and trying to understand its core concepts. Notable examples of such reactions are the Grignard, Diels-Alder, and Wittig reactions; all three played essential roles in the development of chemical synthesis throughout the last century. Emerging as potent synthesis tools in the latter part of the twentieth century, a new class of reactions based on transition metal catalysts formed carbon-carbon bonds. The most notable of these are the palladium-catalyzed cross-coupling processes. This recently learned capacity to form carbon-carbon bonds between or within functionalized and sensitive substrates, based on transition-metal catalysis, opened up new possibilities in many fields, including total synthesis, medicinal and process chemistry, chemical biology, nanotechnology, and total synthesis. Among complete synthesis processes, the Heck, Stille, Suzuki, Sonogashira, Tsuji-Trost, and Negishi reactions using palladium are the most often used to generate carbon-carbon bonds.

The Heck reaction-a palladium-catalyzed coupling of alkenes with aryl, benzyl, and vinyl halides-remains a hot topic in the chemical world due to the wide variety of products it may lead to. Many useful conjugated structures in materials science, as well as natural products, medicines, polymers, and dendrimers, have been synthesized via the Heck reaction.

Particularly urgent and requiring excessive amounts of reactive reagents is the conversion of aldoximes to primary amides. Due to the presence of nitriles, carboxylic acids, and aldehydes as by-products, the selectivity toward the production of the main amide of interest is often rather poor. For most commercial uses, this is seen as a major negative. Only a few number of transition metal salts and complexes have been found so far that can convert aldehydes to amides; they include, $Rh(OH)_x/Al_2O_3$, $[Ir(Cp)Cl_2]_2$, $Pd(OAc)_2$, $In(NO_3)_3/ZnCl_2$, $TerpyRu(PPh_3)Cl_2$, and $FeCl_3$. The documented techniques all have their pros and cons, but the common issues include lengthy reaction durations, the use of expensive and harmful metal salts or ligands, and the use of organic solvents that aren't desirable.

Much current organic chemistry has shifted its attention towards developing environmentally benign and sustainable synthetic methodologies. Typical transition metal-catalyzed reactions, although very efficient, may be based on toxic organic solvents and phosphine-based ligands, which cause concerns in terms of cost, toxicity, and environmental impact. The Heck reaction, one of the key reactions in the formation of carbon-carbon bonds, has found much use in the construction of complex organic molecules, but its conventional forms need non-aqueous conditions and catalysts that are sensitive to air. Over the recent years, water has been considered as a very appealing green solvent to be used in the model of transforming organic reactions with merits like safety, economical nature, and compatibility with the environment.

In this paper, a new palladium complex, Pd[(L)Proline] 2, was prepared and used as an aqueous and microwave-stable phosphine-free catalyst to perform the Heck reaction. The catalytic system was used to facilitate the process of arylation and benzylation of alkenes efficiently without using toxic solvents/ligands. In addition to this, complementary green synthetic methods were also invented such as a Sc(OTf) 3-catalyzed one-pot synthesis of primary amides in water, and a solvent-free, solid-supported reaction to form 2H-indazolo[2,1-b]phthalazinetrinetrione derivatives using KHSO 4-SiO 2. These methods do not only make it easier to conduct reaction processes, but also show the feasibility of green chemistry in high yields, shorter reaction times and catalyst recyclability.

Literature Review

A number of organic compounds with great biological promise have been prepared using scandium (III) trifluoromethanesulfonate [Sc (OTf)3] as a Lewis acidic catalyst in recent years. This catalyst is effective in forming carbon-carbon and carbon-heteroatom bonds, and it is mild, commercially available, inexpensive, and water tolerant. This study compiles the most recent findings on organic transformations catalyzed by Sc (OTf)3, focusing on reactions that produce bonds between carbon atoms and heteroatoms, as published in the previous ten years. Bubun *et al*. (2017) [1].

Here we describe an easy way to make unsymmetrical ethers by reductively etherifying carbonyl compounds with alcohols utilizing 1,1,3,3-tetramethyldisiloxane and a catalytic quantity of scandium (III) triflate (Sc(OTf)3). The reaction produced the necessary products in good to outstanding yields while taking place under moderate room temperature conditions and accommodating a wide variety of substrates, including α, β-unsaturated aldehydes. Specifically, the amount of Sc(OTf)3 catalyst was decreased to 0.1 mol%. Noriyuki *et al*. (2024) [2].

One important aspect of green chemistry that helps the economy and the environment is catalysis. A number of advantages may be gained by the development and use of new, safer catalysts as opposed to older, more harmful ones. These include reduced energy consumption, easier purification processes, more selectivity, and the avoidance of pollution. The majority of green materials used in catalytic applications include various polymers, biopolymers, and clay materials. This chapter provided a synopsis of the use of these environmentally friendly materials in different catalytic reactions. Heterogeneous catalysts made of these environmentally friendly materials have great potential for recovery and reusability in a variety of catalytic processes. Anchal *et al*. (2021) [3].

Methodology

Materials and Methods

Include

- Sources and purity of reagents (Aldrich, Merck, etc.)
- Equipment: CEM microwave reactor, TLC, NMR, IR.
- Solvents: water, EtOAc, MeOH.

Synthesis of $Pd[(L)Proline]_2$

To a solution of L-proline (4.34 mmol, 499 mg) in MeOH (10 mL), 0.6 mL of triethyl amine (Et_3N) was added along with 600 µL of rapidly agitated medium. Then, after 30 minutes of stirring, 2.17 mmol (487 mg) of Pd $(OAc)_2$ was added to the mixture, which was then stirred at room temperature for five hours in a nitrogen atmosphere. After the reaction was finished and identified by TLC, the precipitated complex was filtered, washed with 2 X 2 mL of MeOH, and then dried to g*et al*most quantifiable yield of pure Pd[(L)Proline].

$Pd[(L)Proline]_2$

The substance is a pale greenish solid with the following infrared absorption spectra: 3447, 3075, 2934, 2862, 2510, 1624, 1442, 1351, 1311, 1213, 1082, 929, 863, 777, 649, 545 cm^{-1}.

The ^1H NMR spectrum (300 MHz, D2O) shows many coupling constants: 1.61 (br s, 2H), 1.75-2.01 (br m, 4H), 2.09-2.12 (br m, 2H), 3.03 (br s, 4H), and 3.70-3.88 (br m, 2H) ppm.

The ^{13}C NMR spectrum at 75 MHZ in water shows chemical shifts of 25.6, 25.8, 30.4, 30.8, 52.1, 53.7, 64.5, 65.9, 187.5, and 189.1 ppm.

Microwave-assisted Heck reaction: General procedure

A 10 mL pressured container with a safe pressure control system was used to combine aryl/benzyl halide 1 (1 mmol), alkene 2 (2 mmol), $Pd[(L)Proline]_2$ complex (0.01 mmol, 3 mg, 1 mol%), TBAB (1 mmol, 322 mg, 100 mol%), and NaOAc (0.1 mmol, 8 mg, 10 mol%) with water (1 mL). Using a'snap-on' cover to seal the vial, it was subjected to radiation in a single-mode CEM microwave reactor for 10-50 minutes at temperatures ranging from 80 to 140 °C and power levels of 200 to 300 W. Once the reaction was finished (as shown by TLC monitoring), 3. Three ten millilitre quantities of EtOAc were used for extraction after the mixture was cooled to room temperature. The mixed organic phase was dried over anhydrous Na2SO4, filtered, and solvent removed under vacuum. considered complete. The pure product 3 was obtained by column chromatography purification of the residue.

Microwave-assisted one-pot amide synthesis: General procedure

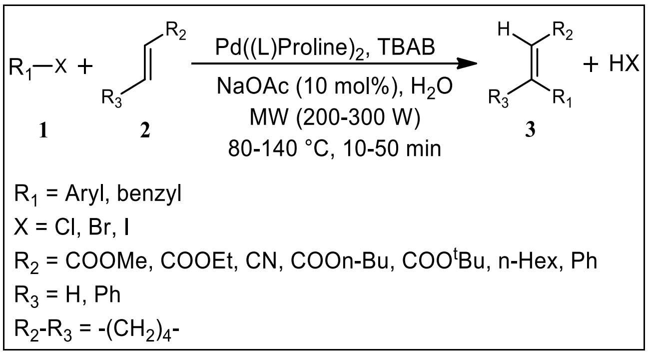
A 10 mL pressured vial with a safe pressure regulator contained 49 mg of $Sc(OTf)_3$, 1 mmol of aldehyde, 1 mmol of NH2OH·HCl, 69 mg of Na_2CO_3, and 1 mmol of Na_2CO_3. The vial was placed in a single-mode CEM Discover Bench Mate microwave reactor and subjected to radiation at 300 W and 135 °C for 15-35 minutes after being sealed with a "snap-on" lid. With regular TLC monitoring, the reaction was halted when the liquid cooled to room temperature. Then, 10 mL of EtOAc was added three times for the extraction process. Following filtration, the solvent was removed by vacuum, and the organic phase mixture was dried over anhydrous Na2SO4. The residual residue was described using physical and spectral data. It was purified using column chromatography on silica gel with EtOAc/hexane as the eluent.

General Experimental Procedure

An aqueous solution containing 1.2 mmol of aldehydes 1, 1 mmol of dimedone 2, 1 mmol of phthalhydrazide 3, and 100 mg of KHSO4-SiO2 was heated in a 25 mL round bottom flask under TLC monitoring at 80 °C for 10 minutes. Once the mixture had cooled to room temperature, it was filtered through Celite using suction after stirring in 30 mL of ethyl acetate. After rinsing with 10 mL of cold water, drying over anhydrous Na2SO4, and finally evaporating under vacuum, the filtrate was purified to get product 4. The residue that resulted from this was then recrystallized from ethanol.

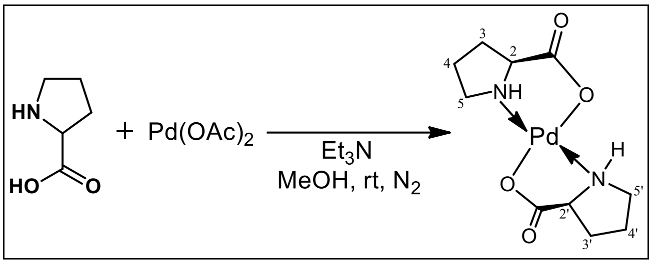
Results and Discussion

Keeping all of that in mind, and because we're still interested in MAOS, we provide here the first-ever use of the $Pd[(L)Proline]_2$ complex as a catalyst for the controlled microwave-assisted arylation and benzylation of alkenes in the presence of tetrabutylammonium bromide and sodium acetate in water. The catalyst is air-stable, efficient, and water-soluble. Use of hazardous organic solvents or phosphorus ligands is not necessary for the process.



Scheme 1: Alkenes undergo Heck reactions with aryl/benzyl halides.

As seen in Scheme 2, the palladium complex was produced by following the process.



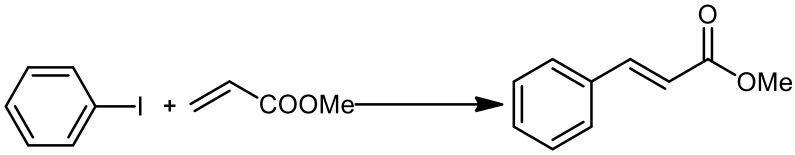
Scheme 2: The $Pd[(L)Proline]_2$ complex is prepared.

^{1}H NMR analysis was used to ascertain the coordination state of the $Pd[(L)Proline]_2$ complex. Thankfully, when contrasted with pure L-proline, all of the proton signals moved along a specific scale, suggesting that the palladium ion was coordinating with the L-proline. In addition, there were no proton signals of acetate in the ^{1}H NMR spectrum, which indicates that the two acetates of $Pd(OAc)_2$ were replaced. The FT-IR spectra of $Pd[(L)Proline]_2$ showed two prominent peaks at 1624 and 1351 cm^{-1}, which are ascribed to the $v_{as}(COO)$ and $v_s(COO)$ of the carboxyl group, respectively. The monodentate coordination of the carboxyl group to the palladium ion is shown by the wider gap between the two peaks ($\Delta = 1624\text{-}1351 = 273\ cm^{-1}$) than 200 cm^{-1}. After obtaining the palladium complex, we set out to test its ability to catalyze the Heck reaction in water.

A thorough investigation was carried out to determine the reaction conditions for the Heck reaction by adjusting various factors (Table 1). Water served as the reaction media in a simulated reaction with iodo benzene and methyl acrylate as substrates. No discernible conversion was seen in the first two efforts utilizing a 0.5 mol% $Pd[(L)Proline]_2$ complex and a 160 W MW power for 5 minutes at 80 or 120 °C (Table 1, entries 1 and 2). The reaction profile remained unchanged when different concentrations of tetrabutylammonium bromide were added and when the temperature was varied (Table 1, entries 3-6). With an increase of 1 mol% for $Pd[(L)Proline]_2$ and 50 mol% for tetrabutylammonium bromide, a yield of 15% for alkene 3a was noted (Table 1, entry 7).

Table 1, entry 8 shows that the product yield was improved to 25% after increasing the tetrabutylammonium bromide concentration to 100%. This was done in an effort to further enhance the yield. Additionally, the impact of changing the MW power, temperature, and duration was examined. Table 1, entry 9 shows that alkene 3a was generated at a 37% concentration after 10 minutes of microwave irradiation at 80 °C and 200 W. The optimal product yield (94%, Table 1, entry 16) was finally achieved by adjusting the base (NaOAc) concentration. Increasing the reaction time, temperature, or MW power did not increase the product yield.

Table 1: Optimization of Heck Reaction Parameters



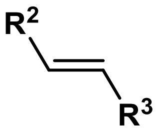
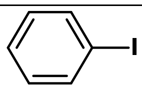
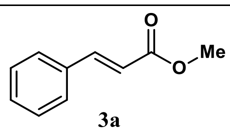
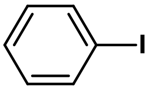
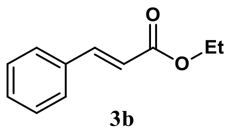
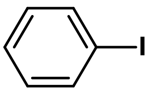
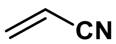
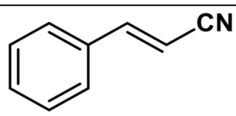
1a 2a 3a

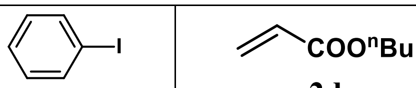
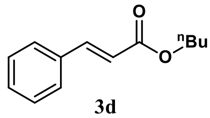
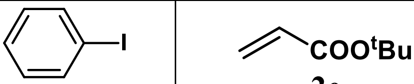
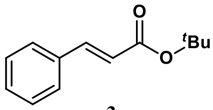
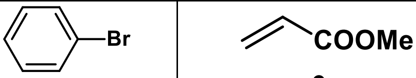
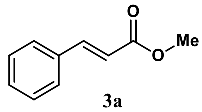
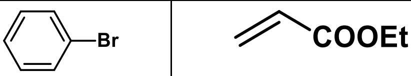
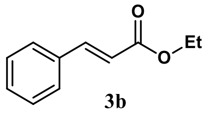
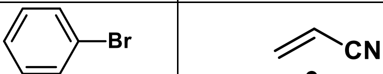
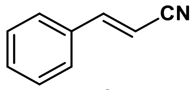
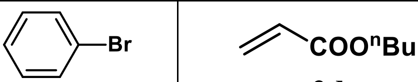
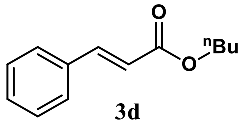
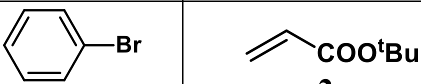
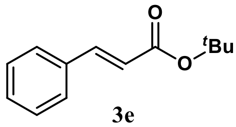
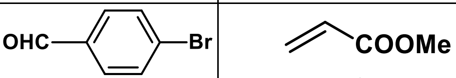
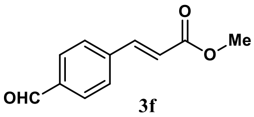
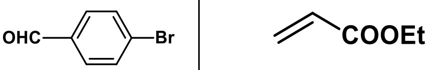
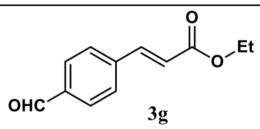
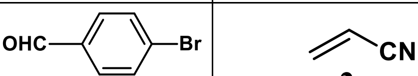
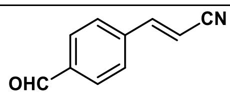
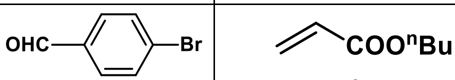
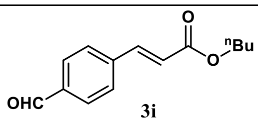
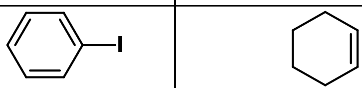
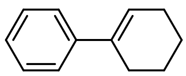
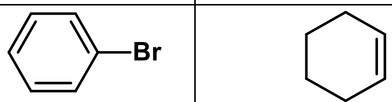
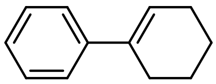
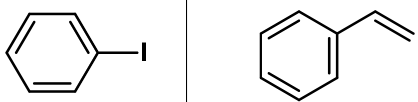
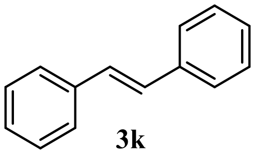
Entry	Pd[(L)Proline]$_2$	TBAB (mol%)	NaOAc (mol%)	Power (W)	Temp (°C)	Time (min)	Yield (%)[a]
1.	0.5	0	0	160	80	5	–
2.	0.5	0	0	160	120	5	–
3.	0.5	50	0	160	80	5	–
4.	0.5	50	0	160	120	5	–
5.	0.5	100	0	160	80	5	–
6.	0.5	100	0	160	120	5	–
7.	1	50	0	160	120	5	15
8.	1	100	0	160	80	5	25
9.	1	100	0	200	80	10	37
10.	1	100	0	200	100	10	35
11.	1	100	0	300	80	10	36
12.	1	100	1	200	80	10	50
13.	1	100	3	200	80	10	63
14.	1	100	5	200	80	10	72
15.	1	100	7	200	80	10	79
16.	1	100	10	200	80	10	94
17.	1	100	10	200	60	10	68
18.	1	100	10	300	80	10	92
19.	1	100	20	200	80	10	94
20.	1	100	10	200	100	10	90
21.	1	200	10	200	80	10	91
22.	1	100	10	200	80	20	93
23.	2	100	10	200	80	10	94

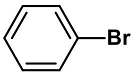
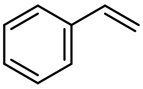
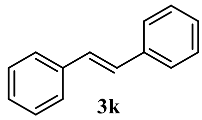
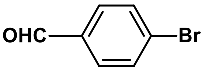
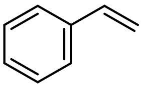
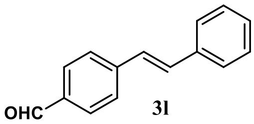
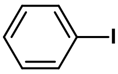
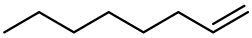
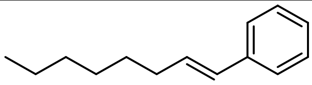
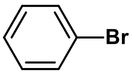
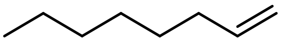
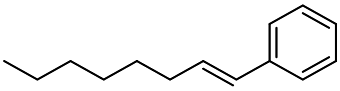
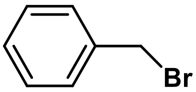
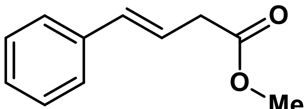
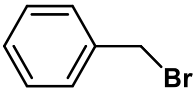
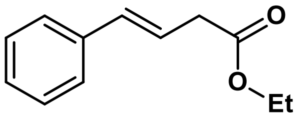
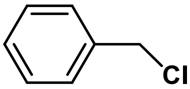
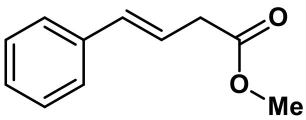
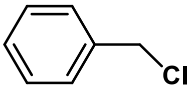
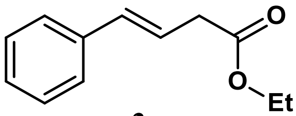
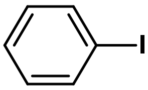
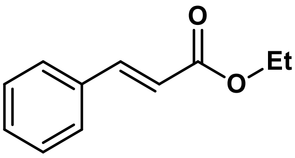
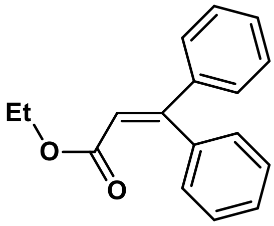
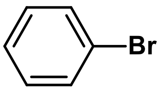
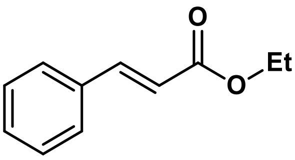
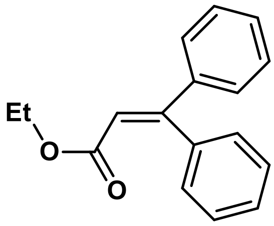
[a]Yield based on iodobenzene.

The yield is dependent on iodobenzene. Afterwards, aryl and benzyl halides 1a-e were subjected to the Heck reaction with activated and unactivated olefins 2a-i in a 1:2 molar ratio. Pd[(L)Proline]$_2$ (1.0 mol%), tetrabutylammonium bromide (100 mol%), and sodium acetate (10 mol%) were used in water along features a "snap-on" top and a pressurized vial for safe management of pressure. Variations in microwave power, temperature, and response time are shown in Table 2. Once the reaction was finished, the products 3a-p were separated and cleaned up using column chromatography. Their physical and spectral properties were afterwards studied.

Table 2: The Heck Reaction for Aryl and Benzyl Halides with Alkenes 2a-i.a. Catalyzed by Pd[(L)Proline]$_2$

Entry	R¹—X		Power (W)	Temp (°C)	Time (min)	Product	Yield (%)[b]
1.	 1a	 2a	200	80	10	 3a	94
2.	 1a	 2b	200	110	20	 3b	90
3.	 1a	 2c	200	110	25	 3c	92

4.	 1a	2d	200	120	20	 3d	91
5.	 1a	2e	300	125	25	 3e	89
6.	 1b	2a	300	135	35	 3a	87
7.	 1b	2b	300	140	50	 3b	83
8.	 1b	2c	300	135	30	 3c	85
9.	 1b	2d	300	135	35	 3d	86
10.	 1b	2e	300	140	40	 3e	85
11.	 1c	2a	300	130	20	 3f	88
12.	 1c	2b	300	130	35	 3g	87
13.	 1c	2c	300	130	30	 3h	85
14.	 1c	2d	300	125	20	 3i	86
15.	 1a	2f	300	135	25	 3j	79[c]
16.	 1b	2f	300	135	25	 3j	77
17.	 1a	2g	300	135	20	 3k	90

18.	 1b	 2g	300	135	25	 3k	85[c]
19.	 1c	 2g	300	135	25	 3l	87
20.	 1a	 2h	300	140	15	 3m	86
21.	 1b	 2h	300	140	25	 3m	83
22.	 1d	 2a	300	135	20	 3n	80
23.	 1d	 2b	300	135	20	 3o	84[c]
24.	 1e	 2a	300	135	30	 3n	78[c]
25.	 1e	 2b	300	135	30	 3o	81[c]
26.	 1a		200	130	20	 3p	86
27.	 1b		200	130	25	 3p	84

[a] One molecular weight of aryl/benzyl halide, two moles of alkene, zero millimoles of Pd[(L)Proline]2, one molecular weight of TBAB, and one memolecular weight of NaOAc.
[b] Isolated yield after aryl/benzyl halide column chromatography 1.
[c] A base concentration of 0.3 mmol was used for the reaction.

Figure 1 depicts a possible process for the production of product 3, based on product isolation and previous research.

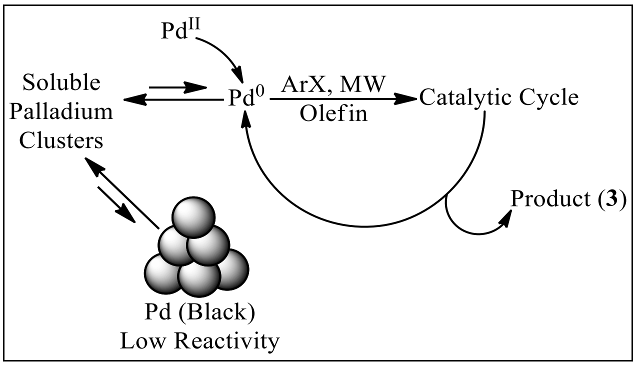
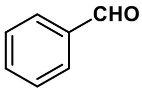
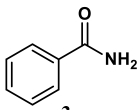
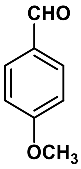
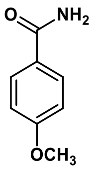
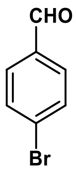
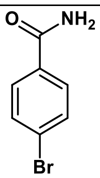
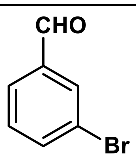
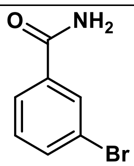
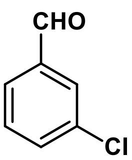
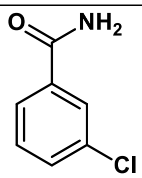


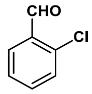
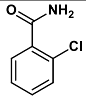
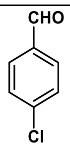
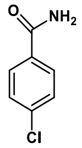
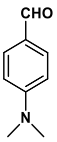
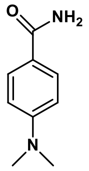
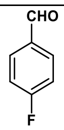
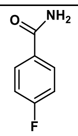
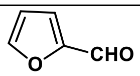
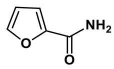
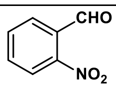
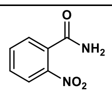
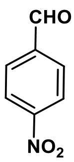
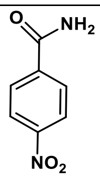
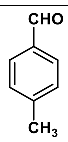
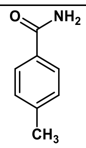
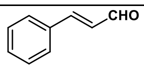
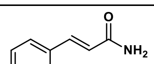
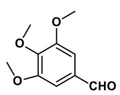
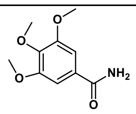
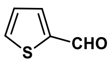
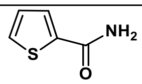
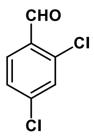
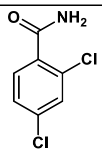
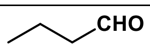
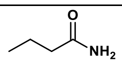
Fig 1: A plausible process for the production of three

Under reflux or MW conditions, none of the other catalytic systems tested, including CAN/Na_2CO_3 and CeCl3·7H2O/Na_2CO_3, enhanced the reaction. Entries 5, 6, 7, and 11 show that using MnCl2·4H2O/Na2CO3, PTSA/Na_2CO_3, P2O5/Na_2CO_3, and CdCl2/Na_2CO_3, a little amount of the desired product was seen under reflux, and under MW, the product yield was somewhat improved. Additionally, under conventional circumstances, the yields of silica sulfuric acid/Na_2CO_3, GaCl3/Na_2CO_3, and LiClO4/Na2CO_3 were poor, with only a little improvement under MW (entry 8, 12, 13). Using 10 mol% Sc(OTf)$_3$ with 100 mol% Na_2CO_3 as a catalyst in water resulted in an impressively high product yield of 92% under reflux conditions (18 h) and 94% under controlled microwave irradiation (300 W, 135 °C, 30 min)-a result that caught us completely off guard (entry 15). It should be noted that Sc(OTf)$_3$ exhibits remarkable resistance to water.

No amount of experimenting with various solvents, bases, and catalyst molar concentrations under both conventional and MW conditions increased the product yield. To extend the reaction's scope, the optimized set of reaction conditions was used to cause a variety of aldehydes (1a-1r) with distinct structural characteristics to react with hydroxylamine hydrochloride. Consequently, high yields (82-95%, entries 1-17) of the relevant primary amides (3a-3r) were achieved. Isolated and purified by column chromatography, the three final products (3a–3r) were further described using physical and spectral data collected after the reaction had finished.

Table 3: A one-pot process for producing primary amides from aldehydes in water catalyzed by Sc(OTf)$_3$.

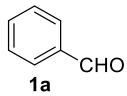
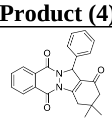
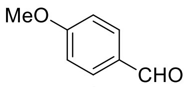
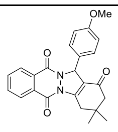
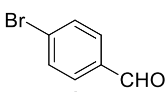
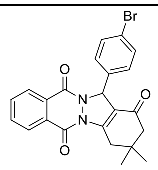
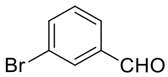
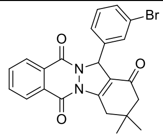
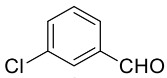
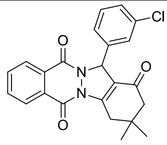
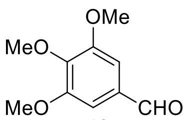
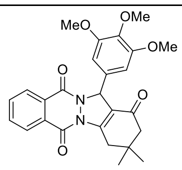
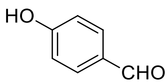
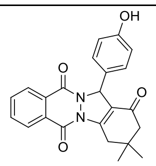
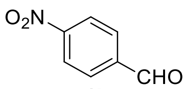
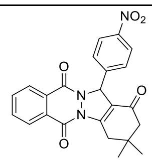
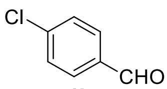
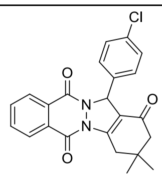
Entry	Substrate	Product	Conventional		Microwave	
			Time (h)	Yield^b (%)	Time (min)	Yield^b (%)
1.	 1a	 3a	18	92	30	94
2.	 1b	 3b	11	86	15	89
3.	 1c	 3c	19	84	30	88
4.	 1d	 3d	21	83	35	86
5.	 1e	 3e	20	87	35	90

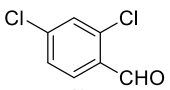
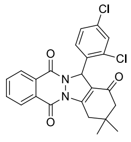
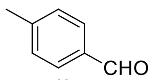
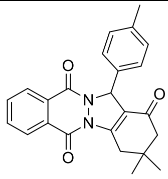
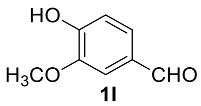
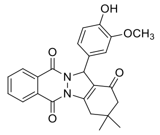
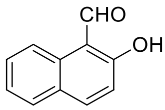
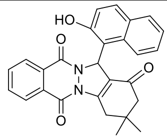
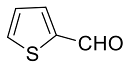
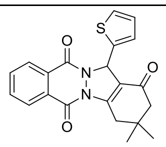
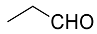
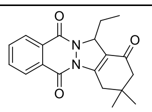
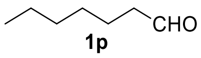
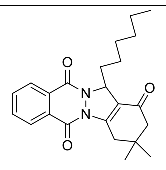
6.	 1f	 3f	24	82	40	85
7.	 1g	 3g	18	79	30	82
8.	 1h	 3h	15	86	15	87
9.	 1i	 3i	20	85	27	91
10.	 1j	 3j	4	90	15	90
11.	 1k	 3k	10	89	20	92
12.	 1l	 3l	7	90	20	95
13.	 1m	 3m	22	81	30	85
14.	 1n	 3n	26	83	27	83
15.	 1o	 3o	16	86	30	89
16.	 1p	 3p	8	89	17	91
17.	 1q	 3q	18	85	25	90
18.	 1r	 3r	12	87	20	92

[a] As a result of reactions carried out in water with 10 mol% $Sc(OTf)_3$ and 1 equiv Na_2CO_3 [100 °C when subjected to reflux and 135 °C when subjected to MW (300 W).
[b]Purified output after crude product column chromatography.

Table 4 summarizes the results of applying the optimal set of reaction conditions to the synthesis of dimedone, phthalhydrazide, and different aldehydes. The reaction proceeded without a hitch, producing products in decent to great yields, from aromatic aldehydes including functional groups like methoxy, bromo, chloro, hydroxy, and nitro to aliphatic aldehydes like acetaldehyde and heptanal. One benefit of our technology is that the catalyst may be reused. The catalyst was extracted by filtering after the reaction was finished, and to the combination of reactants, ethyl acetate was introduced. There is no discernible loss in catalytic activity when reusing the recovered catalyst up to three times after washing with ethyl acetate and drying in the oven (Table 4, entry 1).

Table 4: 2H-indazolo[2,1-b] phthalazine Trione derivatives synthesized in a single step using $KHSO_4$-SiO_2.

Entry	Aldehyde (1)	Product (4)	M.P. (lit) (°C)	Yield[b]
1	 1a	 4a	204-205 (204-206)[29]	94[c]
2	 1b	 4b	221-223 (220-222)[35]	91
3	 1c	 4c	262-264 (265-267)[29]	92
4	 1d	 4d	226-228 (224–226)[37]	90
5	 1e	 4e	206-208 (204-206)[34]	89
6	 1f	 4f	232-235 (232-234)[34]	90
7	 1g	 4g	222-225 (225-227)[36]	92
8	 1h	 4h	224-226 (223-225)[29]	90
9	 1i	 4i	264-267 (262-264)[29]	92

10	 **1j**	 **4j**	218-221 (219-221)[34]	87
11	 **1k**	 **4k**	226-228 (227-229)[29]	90
12	 **1l**	 **4l**	249-251 (250-252)[34]	90
13	 **1m**	 **4m**	159-162 (156-160)[38]	90
14	 **1n**	 **4n**	219-221 (218-220)[35]	87
15	 **1o**	 **4o**	144-147 (145-147)[31]	65
16	 **1p**	 **4p**	85-87 (82-85)[31]	70

[a] following reaction conditions were used: 1 (1.2 mmol), 2 (1 mmol), 3 (1 mmol), 100 mg of $KHSO_4$-SiO_2, 80 °C, and 10 minutes.
[b] Specific yield determined via phthalhydrazide.
[c] the observed yields in the second and third cycles of the reused catalyst are 93% and 91%, respectively.

Conclusion

To sum up, the study was able to testify to a set of green and efficient synthetic procedures, using eco-friendly reaction media and catalysts. The Pd[(L)Proline] 2 complex which was newly synthesized was found to be a good phosphine free catalyst in the Heck reaction in water and yielded good results with microwave irradiation without the need to add complexities in the overall operation and stability of the catalyst. A further step in demonstrating the efficiency of using water as a solvent in microwave-assisted synthesis of primary amides was the microwave-assisted one-pot synthesis of primary amides using $Sc(OTf)_3$ which provided a high yield of products and reaction rates. In this manner, the 2H-indazolophthalazinetrione derivatives produced under the influence of $KHSO_4$-SiO_2 catalysts were an easy, solvent-free and recyclable pathway to the synthesis of heterocyclic compounds.

All these findings contribute to the overall significance and possibility of applying green chemistry concepts to synthetic organic processes. The strategies that will be outlined below offer the alternatives to traditional protocols that are sustainable and will ensure waste reduction, elimination of harmful reagents, and increased catalytic efficiency. The current paper has added to the development of environmentally friendly organic synthesis and has paved the way into the future of pharmaceutical and material chemistry.

References

1. Banerjee, Bubun. (2017). Sc(OTf)3 catalyzed carbon-carbon and carbon-heteroatom bond forming reactions: A review. ARKIVOC: archive for organic chemistry. 2017. 1-25. 10.3998/ark.5550190.p009.868.
2. Nobuta, Tomoya & Mineno, Tomoko & Yamagwa, Noriyuki. (2024). Scandium(III) Triflate-Catalyzed Reductive Etherification of Carbonyl Compounds with Alcohols Using 1,1,3,3-Tetramethyldisiloxane as the Reducing Agent. Synlett. 10.1055/a-2493-7449.

3. Kumari, Pratibha & Lal, Seema & Singhal, Anchal. (2021). Advanced applications of green materials in catalysis applications. 10.1016/B978-0-12-820484-9.00022-2.
4. Prabhu, D.. (2022). Role of Catalysis in Sustainable Chemistry and Conservation of Environment. 10.9734/bpi/pcsr/v1/2171B.
5. Marjadi, Dr & Dr.M.Sulochana, & Mahalle, Dr & Kanimozhi, Dr & N, Dr & Niloufer, Shaheda. (2024). Development of Novel Catalysts for Sustainable Organic Synthesis. Nanotechnology Perceptions. 1505-1522. 10.62441/nano-ntp.vi.2971.
6. Wu, Yufei. (2024). Development and Application of Green Catalysts: Challenges, Optimization, and Future Perspectives. Highlights in Science, Engineering and Technology. 116. 308-314. 10.54097/3mn50856
7. Kim, Yiram & Li, Chao-Jun. (2020). Perspectives on green synthesis and catalysis. Green Synthesis and Catalysis. 1. 10.1016/j.gresc.2020.06.002.
8. Vekariya, Rajesh & Patel, Kinjal & Vekariya, Mayur & Prajapati, Neelam & Rajani, Dr Dhanji & Rajani, Smita & Patel, Hitesh. (2017). Microwave-assisted green synthesis of new imidazo[2,1-b]thiazole derivatives and their antimicrobial, antimalarial, and antitubercular activities. Research on Chemical Intermediates. 43. 1-25. 10.1007/s11164-017-2985-5.
9. Dileep, R.. (2019). An Ionic Liquid Immobilized Palladium Complex for an Effective Heck and Suzuki Coupling Reactions. Chemistry Africa. 2. 1-8. 10.1007/s42250-018-00038-7.