# Chapter 12 Atom Economic Green Organic Reactions



Mohan Neetha, Sankaran Radhika, and Gopinathan Anilkumar

# **1** Introduction

The construction of organic molecules with giant complex structures was a big challenge to synthetic organic chemists from past decade itself. Even though considerable methods provide such complex compounds, the problem associated with these were severe starting material consumption and waste production. Synthetic chemists were in search for reactions which reduced waste generation and consumed minimum raw materials, and afforded good efficiency and selectivity. This point of question can only be solved, when the starting materials are completely consumed to synthesize the desired product alone. This context arouses the opinion of atom economy as the second principle of green chemistry.

Among the twelve principles of green chemistry, the second principle emphasizes the conversion efficiency of reactions. Simply, atom economy is the most generally used metric to calculate the efficiency [1, 2] of greener reactions. Trost has popularized the concept of atom economy [3], which gives the idea that each atom of every starting material being employed or utilized is incorporated in the main product of the chemical reaction, i.e., for a protocol to be 100% atom economic, whole atoms in the reactant should be converted to the desired product and result in minimal waste production. It is measured as follows [4]:

Atom economy = (molecular weight of desired product/molecular weight of all products)  $\times 100\%$ 

e-mail: anilgi1@yahoo.com

201

M. Neetha · S. Radhika · G. Anilkumar (🖂)

School of Chemical Sciences, Mahatma Gandhi University, Priyadarsini Hills, Kottayam, Kerala 686560, India

M. Neetha e-mail: neethamohan131144@gmail.com

S. Radhika e-mail: radhikasreekrishna@gmail.com

<sup>©</sup> Springer Nature Singapore Pte Ltd. 2021

G. Anilkumar and S. Saranya (eds.), *Green Organic Reactions*, Materials Horizons: From Nature to Nanomaterials, https://doi.org/10.1007/978-981-33-6897-2\_12

From the equation, it is evident that hundred percentage atom economy of a reaction could be achieved, only if the desired product alone is formed.

The combination of one pot, atom economic and step economic (PASE) organic synthesis is also found to be significantly greener. Such reactions are important path in the synthesis of various crowded tetrahydropyran-4-ones [5].

From a much simpler and transparent angle, the various atom-economic green reactions are segregated into catalyst-free, water-assisted, pericyclic, solvent-free, ionic liquid-mediated, metal-free dehydrogenative coupling and miscellaneous reactions.

# 1.1 Catalyst-Free Reactions

Bai and co-workers established an innocuous aerobic oxidation of *N*-alkyl iminium salts employing potassium *tert*-butoxide [6]. This protocol is a green approach towards the formation of various lactams from iminium salts of phenanthroline, quinoline, phthalazine, isoquinoline and phenanthridine. The reaction proceeded well under room temperature in the presence of base and solvent without the help of any form of catalysts.

A catalyst-free one-pot green synthetic methodology was used by Mohamadpour for the preparation of dihydropyrano[2,3-c]pyrazole derivatives utilizing glycerol as the reaction media through four-component Knoevenagel–Michael cyclocondensation (Scheme 1) [7]. This high atom economic protocol yielded the product from direct workup procedure without any column separation.

Another catalyst-free protocol for the formation of 3,3'-spirooxindole derivatives by the reaction of a carbonyl compound, malanonitrile and isatins in water was developed by Li et al. [8]. This eco-friendly reaction afforded 18 new 3,3'-spirooxindole derivatives in 75–95% yield. A thermal catalyst-free reaction for the synthesis of 3,3'-spirooxindoles was also reported [9].

A novel one-pot green reaction was reported with isocyanides, alcohols or thiols and elemental sulphur affording *O*-thiocarbamates and dithiocarbamates (Scheme 2)



Scheme 1 Synthesis of dihydropyrano[2,3-c]pyrazoles

Scheme 2 Synthesis of O-thiocarbamates

[10]. This catalyst-free method includes the production of isothiocyanate intermediate, an important scaffold in synthetic chemistry. Good functional group tolerance, moderate to good yields and high atom economy are the major features of this reaction.

# 1.2 Water-Assisted Reactions

 $B(C_6F_5)_3$ -catalysed synthesis of indole-substituted 1,4-naphthoquinones in water was developed by Dong et al. [11]. This high atom economical strategy proceeded via the coupling of 1,4-naphthoquinones with the C-3 position of derivatives of indole (Scheme 3). The reaction could render the desired products in moderate to efficient yields without the aid of any organic solvent and base.

Chate and co-workers developed a synthetic procedure towards benzylpyrazolyl coumarins as well as pyrano[2,3-*c*]pyrazoles integrated by isonicotinic acid hydrazide [12]. 4-Hydroxycoumarin, aldehydes, hydrazine hydrate/phenyl hydrazine hydrate and ethyl acetoacetate reacted together to yield benzylpyrazolyl coumarins whereas pyrano[2,3-*c*]pyrazoles were obtained by the reaction of ethyl acetoacetate, aldehyde, dicyanomethane with isoniazid. Both the reactions were catalysed by 2-aminoethanesulphonic acid in water affording high atom economy.

A novel scheme for quinoline-4-carboxylic acid synthesis via the green Doebner reaction with  $V_2O_5/Fe_3O_4$  as catalyst in water was reported by Khillare and co-workers (Scheme 4) [13]. Catalyst recyclability by simple filtration, short period of reaction, high atom economy, use of water as solvent and less percentage of catalyst are the major attraction of this green Doebner reaction.



Scheme 3 Synthesis of indole-substituted 1,4-naphthaquinones



Scheme 4 Synthesis of quinoline-4-carboxylic acids using V2O5/Fe3O4

Choudhury achieved an effective regioselective base-catalysed synthesis of varieties of new spiro-pyrrolidine-oxindoles using water as the solvent. Isatins, malonitrile and hydantoin or thiohydantoin sequentially reacted in the presence of triethylamine at 70 °C and delivered spirooxindoles tethered with pyrrolizidine unit [14]. A facile lipase-catalysed milder synthetic method to 3,3'-spirooxindoles was reported by Zhang [15]. This novel reaction in water afforded products through Knoevengel–Michael–cyclization, in an eco-favourable manner.

Graphene oxide-catalysed thiolation of indoles was projected as an atom economic strategy by Chen and co-workers [16]. This protocol employed thiols in water for carrying out thiolation, forming 3-sulphenylindoles (Scheme 5). The reaction was performed under organic solvent-free conditions and exhibited wide substrate scope with efficient tolerance towards various functional groups.

Synthesis of various 1,4-disubstituted 1,2,3-triazoles through a one-pot threecomponent reaction was developed by Nasr-Esfahani and co-workers [17]. The reaction between sodium azide and alkynes with  $\alpha$ -bromo ketones or organic halides was catalysed by Cu(II)-TD@nSiO<sub>2</sub> (copper immobilized on nanosilica triazine dendrimer) in (2:1) water:ethanol medium and afforded high atom economy



R = H, 2-Me, 5-NO<sub>2</sub>, 5- CN, 5-OMe

Scheme 5 Substrate scope analysis towards various 3-sulphenylindoles

(Scheme 6). Bis and tris-1,4-substituted 1,2,3-triazoles were also synthesized effectively using the same catalyst.

Nataraj et al. [18] developed a green and highly atom economic synthetic procedure towards N-substituted carbazoles from 2-aminobiaryls. The organic solvent-free and transition metal-free protocol was carried out using peroxodisulphate in water (Scheme 7). The mechanism involved an intramolecular oxidative radical cyclization of the 2-aminobiaryls, resulting in a radical moiety which then underwent an in situ reoxidation.

Brahmachari et al. [19] achieved a green one pot strategy for the synthesis of 3,3'-(arylmethylene)bis(4-hydroxy-2*H*-chromen-2-one), a biologically important biscoumarin derivative, by the reaction of 4-hydroxycoumarin with aromatic aldehydes, utilizing ceric ammonium nitrate (CAN) in aqueous medium at room temperature (Scheme 8). This protocol is cost-effective, environmentally suitable and highly atom economic. Both electron withdrawing and releasing functional groups afforded



Scheme 6 Cu(II)-TD@nSiO<sub>2</sub> catalysed synthesis of 1,4-disubstituted 1,2,3-triazoles, bis and tris-1,4-substituted 1,2,3-triazoles



Scheme 7 Peroxodisulphate catalysed synthesis of N-substituted carbazoles



Scheme 8 Synthesis of 3,3'-(arylmethylene)bis(4-hydroxy-2H-chromen-2-one) in water



Scheme 9 Synthesis of quinolin-2-yl substituted ureas

the products in good yields. The proposed mechanism suggests that both Knoevenagel and Michael-addition reactions are responsible for the conversion of the reactant.

A hundred percentage atom economic and eco-friendly synthesis of different quinolin-2-yl substituted ureas utilizing water as solvent from carbodiimides and quinoline *N*-oxide was disclosed by He et al. [20] (Scheme 9). This base-free condition yielded products in good percentage with excellent regioselectivity via filtration, followed by ethanol washing. Mild reaction conditions, non-toxic raw materials and absence of organic solvents are the other peculiarities of this reaction.

# **1.3** Pericyclic Reactions

Yellappa [21] put forward a one-pot synthesis of indole-spiro(indene-pyrrolidine) via a 1,3-cycloaddition of unsymmetrical dipolarophiles with azomethineylide. The dipolarophile was synthesized from 1-acetyl-1*H*-indol-3-yl derivative and indol-3-yl. The decarboxylative addition of sarcosine, an amino acid, with ninhydrin resulted in the azomethineylide. The protocol exhibited wide functional group tolerance and synthesized different substituted indole-spiro(indene-pyrrolidine) in moderate yields with high atom economy.

A new synthetic avenue towards *trans*  $\beta$ -lactams via an "On water" asymmetric Kinugasa reaction between nitrones and alkynes (Scheme 10) was discussed by Feng and co-workers in 2013 [22]. In contradiction to the ordinary Kinugasa reaction (which carry [3 + 2] cycloaddition reaction of a nitrone with an olefin), high percentage yield of desired products with amazing diastereoselectivity and enantioselectivity were acquired.

$$\begin{array}{c|c} R & R^{1} & H \\ \hline H & H \\ \hline & & \\ \hline & & \\ &$$

Scheme 10 On-water asymmetric Kinugasa reaction

Aqua-mediated stereoselective one-pot synthesis of spiro[acenaphthylene-1,2'thiapyrrolizidine] substituents using NaCl via 1,3-dipolar addition of 1,3-thiazole-4carboxylic acid, acenaphthenequinone and Knoevenagel adduct was established by Dandia [23]. The incorporation of NaCl increased the hydrophobicity of the reaction, which in turn improved the yield of the desired product. The main attraction of this strategy is the formation of four chiral centres consisting of one spiro centre having two C–C and one C–N bonds in a one pot condition, which opens a new area in drug synthesis. Product separation without column chromatography, high atom economy and waste-free isolation of products are the main benefits of this reaction.

Shao and co-workers reported the synthesis of pyrazoles via a  $Bu_4NI$ -catalysed strategy [24]. The major steps involved in this protocol were sequential [3 + 2] cycloaddition and oxidative dehydrogenation reactions (Scheme 11). The reaction exhibited wide substrate scope with easily accessible starting reagents and projected itself as an environmentally innocuous protocol rendering high atom economy.

Quinazolines are pharmaceutically relevant heterocyclic systems exhibiting analgesic, anti-hypertensive, anti-convulsant and anti-histaminic properties [25]. A microwave-assisted green approach towards their synthesis was achieved by a Diels– Alder reaction of 2H-benzo[d][1,3]oxazine-2,4(1H)-dione (isatoic anhydride) with azomethines rendering high atom economy (Scheme 12) [26]. This protocol was more efficient than the conventional synthesis and proceeded at a faster rate providing good to excellent yields of quinazolines.

Mo et al. succeeded in developing a [5 + 1] annulation in water for the synthesis of pyrazino[1,2-a]indole-2-oxides including 2-carbonyl-1-propargylindoles in the presence of hydroxylamine in water with nickel(II) as the catalyst [27]. The oxime intermediate generated from 2-carbonyl-1-propargylindoles and hydroxylamine, underwent a 6-*exo-dig* cyclization catalysed by nickel. The used nickel catalyst was recycled through seven cycles without losing the catalytic efficiency.



Scheme 11 Bu<sub>4</sub>NI-catalysed synthesis of pyrazoles



Scheme 12 Synthesis of substituted quinazoline products



Scheme 13 Diels-Alder reaction using GO as catalyst at room temperature

Graphene oxide (GO)-based Diels–Alder reaction in water was explored by De et al. [28]. This [4 + 2] cycloaddition between 9-hydroxymethylanthracene and *N*-substituted maleimides was feasible at room temperature, when GO is used as carbocatalyst (Scheme 13). The strategy showed many advantages like cost effectiveness, absence of metal catalyst, being a better catalyst than graphene and extensive substrate scope.

#### 1.4 Solvent-Free Reactions

Tufail disclosed a novel malic acid promoted solvent-free Friedlander approach for the construction of polysubstituted quinolones (Scheme 14) [29]. Malic acid as a promoter provided several advantages like high atom economy, broad range of substrate scope and excellent yields.

Pinxterhuis and co-workers explored a solvent-free green Pd-catalysed coupling of organolithium compounds with organic halides [30]. This approach overcomes several challenges that already existed in Pd-catalysed organolithium coupling like removal of humidity, dilution, long reaction period, etc. Even though metal catalysis enhanced atom economy of the reaction, such reactions along with solvent-free conditions significantly improved atom economy furthermore.

A new easy approach to benzothiophene synthesis by the cyclization between thiophenols and alkynes under solvent-free condition was explored (Scheme 15) [31].



Scheme 14 Substrate scope for acyclic  $\alpha$ -methylene compounds



Scheme 15 Synthesis of benzothiophenes through iodine catalysis

This cascade iodine-mediated scheme is inexpensive, efficient and showed reactivity with many functional groups. They could also obtain several benzothiophene frameworks, which are significant in medicinal chemistry in excellent yields. Alkynes having electron-withdrawing substituents resulted in more yield. But thiophenols having electron-withdrawing, releasing and neutral substituents resulted in products without much difference in yields.

Pyrazole-fused 4*H*-pyran and coumarin-fused 4*H*-pyran, namely dihydropyrano[2,3-c]pyrazole pyrano[3,2-c]chromenone were synthesized [32]. Reaction between aromatic aldehydes, (E)-N-methyl-1-(methylthio)-3-methyl-1-phenyl-5-pyrazolone 2-nitroethenamine (NMSM) with or 4hydroxycoumarin under catalyst-free neat conditions accomplished the corresponding products from good to excellent yields. Wide range of substrate study and simple isolation of product are other characteristics of this reaction.

Mirjalili used TiCl<sub>2</sub>/Nano- $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, a new Lewis acid catalyst, along with aldehydes, 1,3-dicarbonyls and ammonium acetate for the one-pot 1,4-dihydropyridines synthesis (Scheme 16) [33]. The condensation in the presence of nano-Lewis acid takes place at 90 °C without any solvent. This greener fruitful reaction is atom economic and superior in selectivity.



Scheme 16 One-pot 1,4-dihydropyridines synthesis

Wells–Dawson diphosphooctadecatungstic acid  $(H_6P_2W_{18}O_{62}\cdot 24H_2O)$  catalysed green synthesis of bis(indolyl)methane analogues under neat conditions was established by Taybee and co-workers [34]. The synthesis involved the electrophilic substitution of a range of carbonyl compounds with indole, providing an excellent atom economic pathway. The reaction of indole with carbonyl compound proceeded via an azafulvenium salt, which then underwent an addition reaction with a second molecule of indole resulting in the bis(indolyl)methane analogues in good to excellent yields.

# 1.5 Ionic Liquid-Mediated Reactions

Sakhalkar et al. explored a novel method for the synthesis of chloroaluminate ionic liquids (ILs), an important catalyst in homogeneous catalysis [35]. Easily accessible starting materials like aluminium chloride and tributylamine provided the desired ionic liquid through an amine–aluminium chloride adduction. This strategy overcomes the problem associated with the conventional method and provided a better atom economy with minimal waste production. The synthesized chloroaluminate ionic liquids were utilized as catalysts for green Friedel–Crafts alkylation reactions.

 $H_2O_2/[TEBSA][BF_4]/CO_4HP_2MO_{15}V_3O_{62}$  catalysed oxidation of various ketones and aldehydes was established by Hu and co-workers [36]. Good to excellent yields of the esters and carboxylic acids were obtained by this mild and facile protocol (Scheme 17). Simple workup procedure and improved catalytic ability with efficient atom economy are the highlights of this reaction.

Brønsted acid ionic liquid (BAIL) catalysed synthesis of 6-amino-4-substituted-3-methyl-2,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitriles was designed by



Scheme 17  $H_2O_2/[TEBSA][BF_4]/CO_4HP_2MO_{15}V_3O_{62}$  catalysed oxidation of aldehydes and ketones



Scheme 18 Synthesis of 6-amino-4-substituted-3-methyl-2,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitriles

Nimbalkar et al. [37]. Triethylammonium hydrogen sulphate  $[Et_3NH][HSO_4]$  was chosen as the BAIL for this strategy and could catalyse the one-pot reaction between aryl aldehydes, hydrazine hydrate, propanedinitrile and ethylacetoacetate under neat conditions (Scheme 18). The reaction proceeded at a faster rate imparting excellent yields with high catalytic recyclability. The synthesized products were active against various cancer cell lines.

Carbon dioxide is very toxic to the environment as well as to the humans. It increases the global temperature of earth significantly. Conversion of carbon dioxide into valuable organic compounds has always gained much attention. Carboxylative cycloaddition of  $CO_2$  to propargylic alcohols is one of the methods for  $CO_2$  fixation [38]. This highly atom economic protocol synthesizes biologically relevant five-membered cyclic carbonates in a single step using metal-, organo-, electrochemical-and ionic liquid-catalysed strategies.

# 1.6 Metal-Free Dehydrogenative Coupling Reactions

Nowadays, metal-free method for cross-dehydrogenative couplings (CDC) is much significant than metal involved CDC reactions. These types of reactions gained attention since they are important in the construction of C–C, C–N, C–O, C–S and C–Se bonds. But molecular iodine catalysed CDC reactions has been noticed as more atom economic and greener with wide range of substrate scope and regioselectivity [39].

An iodine catalysed cyclopropane ring formation was reported by Itoh from aromatic olefins, using active methylene compounds in the presence of visible light (Scheme 19) [40]. Various substituted cyclopropane derivatives were obtained through a carbon–iodine bond breakage mechanism, in moderate to good yields. Usually, styrenes with electron-deficient groups yielded more product yields than those with electron-rich systems.



A tandem approach for the stereospecific formation of *E* and *Z* isomer of 2thio-1,4-enediones with TMSOTf and BF<sub>3</sub>·Et<sub>2</sub>O, respectively, by self-coupling of terminal alkynes was developed by Shah [41]. This iodine catalysed reaction also provided an opportunity for the synthesis of  $\beta$ -thio- $\gamma$ -keto- $\alpha$ , $\beta$ -unsaturated esters via cross-coupling with ethyl glyoxylate. A wide variety of terminal alkynes yielded the desired diones in excellent yields.

Iodine-catalysed  $\beta$ -hydroxysulphide synthesis via the formation of C-O and C-S bonds in one step was reported by Peddinti and co-workers [42]. Readily available styrenes and thiophenols reacted in DMSO affording the corresponding products in good yields (Scheme 20). Starting materials containing halogens and electron-releasing groups afforded better yields of the products. This method is very simple, cost-effective, greener and safe.

Introduction of several aromatic thiols on imidazo[1,2-*a*]-pyridines, -pyrimidines and [1,2-*b*]pyridazines in PEG-400, using molecular iodine as catalyst and  $H_2O_2$  as oxidizing agent was discovered by Hiebel [43]. This sulphenylation method with different thiophenols are effective, facile, regioselective and tolerated many functional groups.

A metal-free molecular iodine-mediated formation of  $\alpha$ -carbonyl selenocyanates, which are important starting materials for biologically active molecules, from aromatic methyl ketones via selenocyanation was reported (Scheme 21) [44]. This method avoids the usage of previously prepared  $\alpha$ -halo ketones. This convenient strategy provided a broad substrate scope study and supplied desired selenocyanates in good yields. Mechanistic study found that, the generation of iodine radical is essential for the progress of this reaction.

Benzamides can be smoothly prepared by domino approach of ethylarenes with aqueous ammonia taking iodine as the catalyst (Scheme 22) [45]. This novel procedure progressed via a triiodomethyl ketone transition state, which is formed from



Scheme 20 Synthesis of  $\beta$ -hydroxysulphides through iodine catalysis



Scheme 21 Formation of  $\alpha$ -carbonyl selenocyanates via iodine catalysis



the oxidant TBHP and iodine. An amide is then formed by the nucleophilic substitution of the intermediate with ammonia. The efficiency of the reaction was confirmed through 17 substrates, which yielded the respective products ranging from 73 to 94%.

A straightforward indoline synthesis from intramolecular amination of anilines was established by Qui (Scheme 23) [46]. This reaction created a novel pathway for the formation of (sp<sup>3</sup>)C–N bonds by the selective breakage of (sp<sup>3</sup>)C–H bonds over (sp<sup>2</sup>)C–H bonds. This iodine-catalysed methodology furnished varieties of heterocycles having nitrogen atom. The proposed mechanism in the study suggested the cleavage of N–I bond.

The single-step oxidative coupling of alkenes with  $\beta$ -keto esters or 2-pyridinyl- $\beta$ -esters, described by Lei et al., is one of the best avenues for the synthesis of dihydrofurans and indolizines, respectively (Scheme 24) [47]. This iodine-mediated annulation was believed to proceed via a radical addition or cyclization mechanism.

A photo-induced selective synthetic route to substituted piperidines using  $(sp^3)C-H$  amination was explored (Scheme 25) [48]. This intramolecular amination path operates through two catalytic cycles, in which the first one is for light-mediated radical C-H abstraction and the other for iodine catalysed C-N bond formation. This protocol also promoted the synthesis of pyrrolidine derivatives, which are commonly prepared through Hofmann–Löffler reaction.



Scheme 23 Selective (sp<sup>3</sup>)C–H functionalization



Scheme 24 Synthesis of dihydrofurans and indolizines



Scheme 25 Iodine-catalysed piperidine formation



Scheme 26 Synthesis of 2-phenylquinazolines

Taking 2-aminobenzophenones and benzylic amines as starting materials, Wang and co-workers described the formation of 2-phenylquinazolines via using iodine as catalyst (Scheme 26) [49]. This reaction is achieved through a tandem pathway, followed by sp<sup>3</sup> C–H functionalization. Electron-releasing groups on the phenyl ring disgraced the reaction yield. *Ortho* substituents disfavour the reaction due to steric hindrance. This novel iodine-catalysed approach has different merits such as metal-free, elimination of toxic reagents, easy availability of reactants; moreover, it is facile and efficient.

# 1.7 Miscellaneous Reactions

A mild and efficient green method towards the fixation of  $CO_2$  was manifested by Garai et al. [50]. Covalent organic polymer (COP-213), a zwitterionic  $\pi$ -conjugated catalyst showcased improved selectivity for the cycloaddition of  $CO_2$  to epoxide and could bring about effective conversion of carbon dioxide to cyclic carbonates in the absence of solvents and co-catalysts.

Singh et al. [51] designed a novel approach for the Rose Bengal catalysed crosscoupling of phenylene, 1,2–dicarbonyls and 1,2–diamines in quinoxaline derivative synthesis (Scheme 27). This protocol was found to take place at room temperature in the presence of visible light via a radical route.

(BMOPs) polybismaleimide-based microporous organic polymers were designed via a green, atom economic initiative [52]. The monomer bismaleimide underwent a one-step thermal-initiation homopolymerization in diphenyl sulphone. The highlights of this reaction include exclusion of any initiator and thereby reducing side product formation. These green specialities pave way to a large-scale production of these polymers for industrial applications.



Scheme 27 Synthesis of quinoxalines via Rose Bengal catalysis

Ji and co-workers designed a procedure towards the synthesis of indoles and pyrrolo[3,2,1-*ij*]quinolones [53]. The metal-free protocol utilized NH<sub>4</sub>PF<sub>6</sub>, a less toxic, economic and safe inorganic salt to promote the synthesis (Scheme 28). The synthesized products obtained after a cyclodehydration were projected as relevant pharmacophores. The process was carried out in HFIP (1,1,1,3,3,3-hexafluoropropan-2-ol) solvent and provided excellent atom-economy.

Pradhan mentioned the preparation of support-free  $Pd_3CO$  nanocomposites, found as a good catalytic system for iodonium ylides with acrylates, boronic acids and arylalkynes, in Heck, Suzuki and Sonogashira cross-coupling reactions, respectively [54]. This coupling is progressed by the movement of phenyl ring together with the formation of  $\alpha$ -iodoenones, as the intermediate and yielded the coupled product with high atom economy. This coupling accesses a new path in the synthesis of diverse organic compounds.



Scheme 28 Synthesis of pyrrolo[3,2,1-ij]quinolines and indoles

# 2 Conclusion

Atom economic reactions play vital roles in the sustainable development, as it goals to bring down the amount of waste in a chemical reaction to a molecular level. High atom economic reactions, obeying greener principles, are safe and efficient. The notion of atom economy basically exhibits the percentage of atoms that is used up in the major product, comparing with the actual no. of atoms initially present in the reaction. So far from the above discussion, it is clear that various modern green organic reactions are highly atom economic and a few of them are hundred percentage atom economic. Scientists of all organic fields are still attempting their best to bring out all reactions to an ideal atom economic situation.

Acknowledgements MN and SR thank the Kerala State Council for Science Technology and Environment (KSCSTE), Trivandrum research fellowships. GA thanks the KSCSTE, Trivandrum, India for a research grant (Order No.341/2013/KSCSTE dated 15.03.2013). The authors are also thankful to EVONIK Industries, Germany for financial support (ECRP 2016 dated 6.10.2016).

# References

- 1. Trost BM (1995) Atom economy—a challenge for organic synthesis: homogeneous catalysis leads the way. Angew Chem Int Ed Engl 34(3):259–281
- Li C-J, Trost BM (2008) Green chemistry for chemical synthesis. Proc Natl Acad Sci 105(36):13197–13202
- 3. Trost BM (1991) The atom economy-a search for synthetic efficiency. Science 254(5037):1471-1477
- Jiménez-González C, Constable DJC, Ponder CS (2012) Evaluating the "Greenness" of chemical processes and products in the pharmaceutical industry—a green metrics primer. Chem Soc Rev 41(4):1485–1498
- 5. Clarke PA, Santosa S, Martin WHC (2007) Combining pot, atom and step economy (PASE) in organic synthesis. Synthesis of tetrahydropyran-4-ones. Green Chem 9(5):438–440
- Bai L-G, Zhou Y, Zhuang X et al (2020) Base-promoted aerobic oxidation of N-alkyl iminium salts derived from isoquinolines and related heterocycles. Green Chem 22(1):197–203
- Mohamadpour F (2019) Four-component synthesis of Dihydropyrano[2,3-c]pyrazole scaffolds using glycerol as green reaction media under catalyst-free conditions. Polycyclic Aromat Compd. https://doi.org/10.1080/10406638.2019.1709084
- Zhao L-Q, Zhou B, Li Y-Q (2011) An efficient one-pot three-component reaction for synthesis of spirooxindole derivatives in water media under catalyst-free condition. Heteroat Chem 22(5):673–677
- 9. Elinson MN, Ilovaisky AI, Merkulova VM et al (2012) Non-catalytic thermal multicomponent assembling of Isatin, cyclic CH-acids and Malononitrile: an efficient approach to Spirooxindole scaffold. Mendeleev Commun 22(3):143–144
- Németh AG, Keserű GM, Ábrányi-Balogh P (2019) A novel three-component reaction between isocyanides, alcohols or thiols and elemental sulfur: a mild, catalyst-free approach towards O-thiocarbamates and dithiocarbamates. Beilstein J Org Chem 15:1523–1533
- 11. Dong Y, Zhang H, Yang J et al (2019)  $B(C_6F_5)_3$ -catalyzed C–C coupling of 1,4-Naphthoquinones with the C-3 position of Indole derivatives in water. ACS Omega 4(25):21567-21577

- 12 Atom Economic Green Organic Reactions
- 12. Chate AV, Shaikh BA, Bondle GM, Sangle SM (2019) Efficient atom-economic one-pot multicomponent synthesis of benzylpyrazolyl coumarins and novel pyrano[2,3-*c*]pyrazoles catalysed by 2-aminoethanesulfonic acid (taurine) as a bio-organic catalyst. Synth Commun 49(17):2244–2257
- Arbad BR, Khillare SL, Lande MK et al (2017) Synthesis, characterization and catalytic application of V<sub>2</sub>O<sub>5</sub>/Fe<sub>3</sub>O<sub>4</sub> as heterogeneous catalyst for the synthesis of Quinoline-4-carboxylic acid derivatives. Der Pharma Chemica 9(6):30–36
- 14. Karamthulla S, Pal S, Choudhury LH et al (2013) Synthesis of novel spiro[indoline-3,7'pyrrolo[1,2-*c*]imidazole]-6'-carbonitrile derivatives in water using a regioselective sequential three component reaction. RSC Adv 3(36):15576–15581
- 15. Chai S-J, Lai Y-F, Xu J-C et al (2011) One-pot synthesis of Spirooxindole derivatives catalyzed by Lipase in the presence of water. Adv Synth Catal 353(2–3):371–375
- Chen M, Luo Y, Zhang C et al (2019) Graphene oxide mediated thiolation of indoles in water: a green and sustainable approach to synthesize 3-sulfenylindoles. Org Chem Front 6(1):116–120
- 17. Nasr-Esfahani M, Mohammadpoor-Baltork I, Khosropour AR et al (2014) Copper immobilized on nanosilica triazine dendrimer (Cu(II)-TD@nSiO<sub>2</sub>)-catalyzed regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles and bis- and tris-triazoles via a one-pot multicomponent click reaction. J Org Chem 79(3):1437–1443
- Natarajan P, Priya CD (2017) Transition-metal-free and organic solvent-free conversion of Nsubstituted 2-aminobiaryls into corresponding carbazoles via intramolecular oxidative radical cyclization induced by peroxodisulfate. Green Chem 19(24):5854–5861
- Brahmachari G, Begam S (2019) Ceric ammonium nitrate (CAN): an efficient and eco-friendly catalyst for one-pot synthesis of diversely functionalized biscoumarins in aqueous medium under ambient conditions. ChemistrySelect 4(19):5415–5420
- Jiang S, Cao Z, He W-M et al (2019) Clean preparation of Quinolin-2-yl substituted ureas in water. ACS Sustain Chem Eng 7(7):7193–7199
- Yellappa S (2019) An anti-Michael route for the synthesis of indole-spiro(indene-pyrrolidine) by 1,3-cycloaddition of azomethineylide with indole-derivatised olefins. J Heterocycl Chem. https://doi.org/10.1002/jhet.3843
- 22. Liu X, Feng X, Chen Z et al (2013) Asymmetric synthesis of trans-β-Lactams by a Kinugasa reaction on water. Chem Eur J 19(23):7561–7567
- 23. Dandia A, Parewa V, Kumar S et al (2016) Imposed hydrophobic interactions by NaCl: accountable attribute for the synthesis of spiro[acenaphthylene-1,5'-pyrrolo[1,2-c]thiazole] derivatives via 1,3-dipolar cycloaddition reaction in aqueous medium. Green Chem 18(8):2488–2499
- 24. Shao Y, Tong J, Zhao Y et al (2016) [3 + 2] cycloaddition and subsequent oxidative dehydrogenation between alkenes and diazo compounds: a simple and direct approach to pyrazoles using TBAI/TBHP. Org Biomol Chem 14(36):8486–8492
- 25. Alagarsamy V, Chitra K, Saravanan G (2018) An overview of quinazolines: pharmacological significance and recent developments. Eur J Med Chem 151:628–685
- 26. Mullasseril A (2013) Substituent effects on solvent-free synthesis (MWAOS) of dihydroquinazolinones by the addition of isatoic anhydride to a series of phenyl-substituted n-(phenylmethylidene) anilines. J Chem 2013:1–4
- Xiao Y, Su G-F, Mo D-L et al (2019) Nickel(II)-catalyzed [5 + 1] annulation of 2-carbonyl-1propargylindoles with hydroxylamine to synthesize pyrazino[1,2-a]indole-2-oxides in water. J Org Chem 84(16):9859–9868
- 28. De M, Girish YR, Pandit S et al (2017) Graphene oxide as a carbo-catalyst for Diels-Alder reaction in aqueous media. Chem Asian J 12(18):2393–2398
- 29. Singh J, Singh J, Tufail F et al (2017) Bioorganopromoted green friedländer: a versatile new Malic acid promoted solvent free approach to multisubstituted quinolones. New J Chem 41(4):1618–1624
- 30. Pinxterhuis EB, Giannerini M, Hornillos V et al (2016) Fast, greener and scalable direct coupling of organolithium compounds with no additional solvents. Nat Commun 7:11698
- Yan K, Yang D, Wang H et al (2015) Facile access to benzothiophenes through metal-free iodine-catalyzed intermolecular cyclization of thiophenols and alkynes. Synlett 26(13):1890– 1894

- 32. Khan MM, Shareef S, Saigala et al (2019) A catalyst- and solvent-free protocol for the sustainable synthesis of fused 4H-pyran derivatives. RSC Adv 9(45):26393–26401
- Mirjalili BBF, Bamoniri A, Salmanpoor LA (2018) TiCl<sub>2</sub>/Nano-γ-Al<sub>2</sub>O<sub>3</sub> as a novel Lewis acid catalyst for promotion of one-pot synthesis of 1,4-dihydropyridines. J Nanostruct 8(3):276–287
- 34. Tayebee R, Nehzat F, Rafiee E et al (2011) An efficient and green synthetic protocol for the preparation of bis(indolyl)methanes catalyzed by H<sub>6</sub>P<sub>2</sub>W<sub>18</sub>O<sub>62</sub>·24H<sub>2</sub>O, with emphasis on the catalytic proficiency of Wells-Dawson versus Keggin heteropolyacids. J Mol Catal A-Chem 351:154–164
- Sakhalkar M, Aduri P, Lande S, Chandra S (2020) Single-step synthesis of novel chloroaluminate ionic liquid for green Friedel-Crafts alkylation reaction. Clean Techn Environ Policy 22:59–71
- Hu Y-L, Li D-J, Li D-S (2015) Efficient and convenient oxidation of aldehydes and ketones to carboxylic acids and esters with H<sub>2</sub>O<sub>2</sub> catalyzed by Co<sub>4</sub>HP<sub>2</sub>Mo<sub>15</sub>V<sub>3</sub>O<sub>62</sub> in ionic liquid [TEBSA][BF<sub>4</sub>]. RSC Adv 5(32):24936–24943
- Nimbalkar UD, Seijas JA, Nikalje APG et al (2017) Ionic liquid-catalyzed green protocol for multi-component synthesis of dihydropyrano[2,3-c]pyrazoles as potential anticancer scaffolds. Molecules 22(10):1628–1644
- Li M, Abdolmohammadi S, Vessally E et al (2020) Carboxylative cyclization of propargylic alcohols with carbon dioxide: A facile and Green route to α-methylene cyclic carbonates. J CO2 Util 38:220–231
- Parvatkar PT, Manetsch R, Banik BK (2019) Metal-Free cross-dehydrogenative coupling (CDC): molecular iodine as a versatile catalyst/reagent for CDC reactions. Chem Asian J 14(1):6–30
- 40. Itoh A, Tada N, Usami K et al (2016) Intermolecular cyclopropanation of styrenes using iodine and visible light via carbon-iodine bond cleavage. Org Lett 18(1):8–11
- 41. Devari S, Kumar A, Shah BA et al (2015) C-H functionalization of terminal alkynes towards stereospecific synthesis of (E) or (Z) 2-methylthio1,4-ene-diones. Chem Commun 51(24):5013–5016
- 42. Tehri P, Aegurula B, Peddinti RK (2017) Iodine-catalysed regioselective synthesis of  $\beta$ -hydroxysulfides. Tetrahedron Lett 58(21):2062–2065
- Hiebel M-A, Berteina-Raboin S (2015) Iodine-catalyzed regioselective sulfenylation of imidazoheterocycles in PEG<sub>400</sub>. Green Chem 17(2):937–944
- 44. Sun K, Lv Y, Wang X et al (2017) A novel metal-free method for the selenocyanation of aromatic ketones to afford  $\alpha$ -carbonyl selenocyanates. Org Biomol Chem 15(20):4464–4467
- 45. Vadagaonkara KS, Prakashb S, Chaskar CA et al (2015) Iodine-mediated domino protocol for the synthesis of benzamides from ethylarenes via sp3 C–H functionalization. Synlett 26(12):1677–1682
- 46. Qiu R, Au C-T, Yin S-F et al (2017) Intramolecular, site-selective, iodine-mediated, amination of unactivated (sp<sup>3</sup>)C-H bonds for the synthesis of indoline derivatives. Org Lett 19(11):2793– 2796
- 47. Gao X, Gao M, Lei A et al (2015) Iodine-catalyzed radical oxidative annulation for the construction of dihydrofurans and indolizines. Org Lett 17(10):2404–2407
- Zhang H, Muñiz K (2017) Selective piperidine synthesis exploiting iodine-catalyzed Csp<sup>3</sup>-H amination under visible light. ACS Catal 7(6):4122–4125
- 49. Zhang J, Yu C, Wang Z (2010) A simple and efficient approach to the synthesis of 2-Phenylquinazolines via sp<sup>3</sup> C–H functionalization. Org Lett 12(12):2841–2843
- 50. Garai M, Rozyyev V, Ullah Z (2019) Zwitterion π-conjugated network polymer based on guanidinium and β-ketoenol as a heterogeneous organo-catalyst for chemical fixation of CO<sub>2</sub> into cyclic carbonates. APL Mater 7:111102–111109
- 51. Sharma AK, Singh J, Singh J et al (2019) Rose Bengal catalyzed coupling of 1,2-dicarbonyls and phenylene 1, 2-diamines: visible-light mediated synthesis of quinoxalines. ChemistrySelect 4(29):8713–8718
- 52. Zhu T, Yu Q, Ding L (2019) Atom-economical Preparation of polybismaleimide-based microporous organic polymers. Green Chem 21(9):2326–2333

- 12 Atom Economic Green Organic Reactions
- Ji X-M, Zhou S-J, Deng C-L et al (2014) NH<sub>4</sub>PF<sub>6</sub>-promoted cyclodehydration of a-amino carbonyl compounds: efficient synthesis of pyrrolo-[3,2,1-*ij*]quinoline and indole derivatives. RSC Adv 4(96):53837–53841
- Pradhan S, Mishra K, Lee YR (2019) Support-free Pd<sub>3</sub>CO NCs as an efficient heterogeneous nanocatalyst for new organic transformations of C–C coupling reactions. Chem Eur J 25(46):10886–10894