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Significant Green Chemistry Metrics: Role of Atom Economy and Reaction Mass Efficiency in ChemicalProcess

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ABSTRACT

As the population of world is increasing enormously, there arise a challenge to develop the ways that address the needs of present generation without compromising the ability of future generation to meet their own needs, such kind of development is called Sustainable development .It results in lowering natural harm and reduces the wastage of resources. Applying such manageable development to chemical industries is simply called as 'GREEN CHEMISTRY'. Its basic idea is to prevent pollution, counteract contamination and production of wastes instead of producing them and tidying them up. There are 12 basic principles of green chemistry that have to be kept in mind while outlining a synthetic process in a greener way. So, then after developing a reaction procedure concerned with all such principles of green chemistry where ever possible and then the next step is to evaluate the greenness of reaction quantitatively, Thus we require certain Metrics/Standards which are generallytermed as green chemistry metrics / simply process chemistry metrics. This formal assessment provides an insight on various metrics so far been introduced and an exhaustive view of importance of Atom economy and Reaction mass efficiency in calculating efficiency of reactions.

Keywords: Sustainable development, Atom economy, Reaction Mass Efficiency, Catalysts.

INTRODUCTION

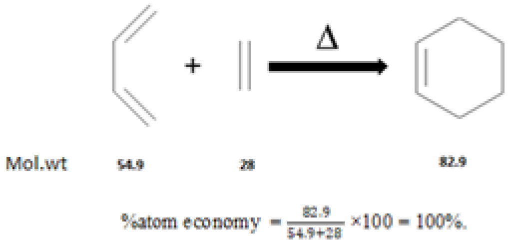
The concept of green chemistry emerged as essential tool for promoting sustainable development in laboratories and industries, For instance, we may have 2 or 3 different methods for synthesis of a substance, the selection of suitable method rely on the process which have usage of less hazardous materials, which are economical, that even reduce production of byproducts and so on. Along with these, maximization of starting material into desired product has gained more popularity to make reaction more economical.

Condensed principles of green chemistry:
P – Prevent wastes
R – Renewable materials
O - Omit Derivatization step
D – Degradable chemical productsU – Use safe synthetic methods
C – Catalytic reagents
T – Temperature, pressure ambientI – In process monitoring
V –Very few auxiliariesE – E- factor
L – Low toxicity of chemical productsY –Yes, it is safe.
Coupled with the need to invent ecofriendly chemical reaction, there is equal need to quantify the greenness of reaction by usingso-called green chemistry metrics.

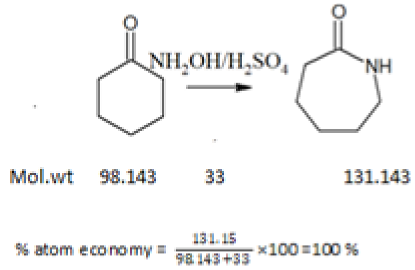
Significant Green Chemistry Metrics Importance Of Green Chemistry Metrics: Process chemistry metrics are a system or standards of measurement of various aspects in a chemical process .They Serves to quantify efficiency of process and allows for easy identification of the best and worst reactions in a process or Sequence. Such relative efficiencies of a reaction help to evaluate convenient synthetic routes of Preparation. These standards rank the greenness of reaction process as quantitative as possible. Number of metrics has been proposed so far to make chemist aware of need to select method which generates less wasteful byproducts. Implementation of these metrics particularly, in pharmaceutical industries is gaining more access as these industries are singled out as the one producing more waste per gram of target product.

A good metric must be clearly defined simple, measurable, and objective rather than subjective. Few of them are:
Percentage yield
E-factor
Mass intensity
Solvent and catalyst environmental impact factorStoichiometric factor
Effective mass yieldCarbon efficiency
Among these metrics the most prominent ones include: Atom economy
Reaction mass efficiency

1. Addition reaction of ethane and butadiene Beckmann rearrangement

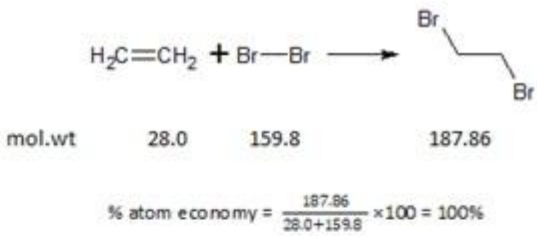


Scheme 1:Atom economy Calculation for Addition Reaction of 1,3 Butadiene and ethene.



Scheme 2:Atom economy Calculation for Rearrangement reaction of Cyclohexanone to Caprolactum.

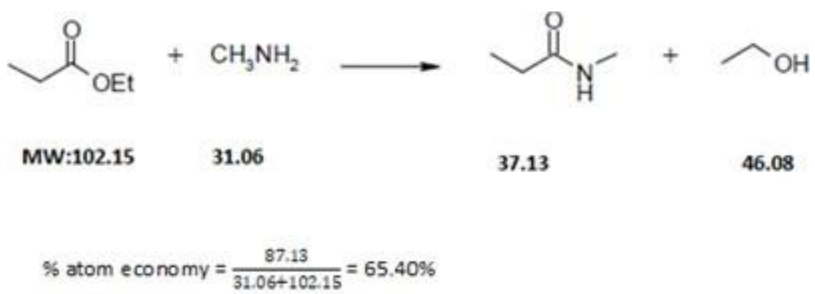
2. Allyl phenyl ether rearrangement to O-alyl phenol.
   Bromination of alkene.



Scheme 4: Atom economy Calculation for Bromination of Alkene

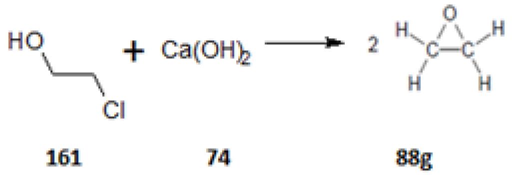
Examples of reactions with reduced A.E due to substitution and elimination types.

3. Substitution of methyl amine and ethyl propionate in amide formation.



Scheme 5: Atom economy Calculation for Substitution Reaction of Methyl Amine and Ethyl propionate

4. Formation of ethylene oxide from 2-chloro ethanol and calcium hydroxide involving elimination of calcium chloride and water.

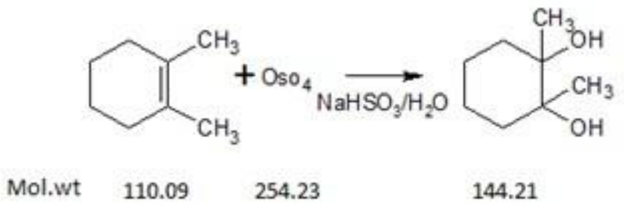


$$\%\text{atom economy} = \frac{88}{161+74} \times 100 = 37.4\%$$

Schem 6:Atom economy Calculation of reaction involved in Synthesis of Ethylene Oxide.

Addition reactions may often not provide 100% atom economy in certain cases one such an example is osmium tetroxide mediateddihydroxylation.

These inefficiencies provide opportunities to design new reactions with the goal of improving atom economy.

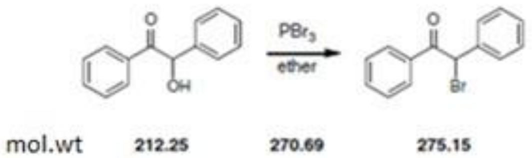


$$\%\text{atom economy} = \frac{144.21}{110.09+254.23} \times 100 = 34\%$$

Scheme 7:Atom economy Calculation of Dihydroxylation Reaction invilving Osmium Tetroxide.

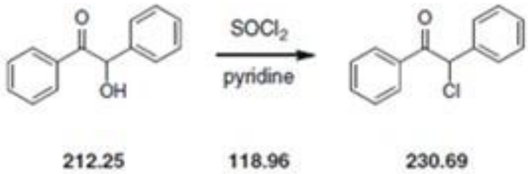
Although such substitution and elimination reactions are intrinsically wasteful, there exist an opportunity to design reaction of better atom economy ex: preparation of alkyl halides from alcohols. Choosing appropriate substituent depends on gaining accessto better leaving group for further reaction or step with high atom economy.

Ex: below reactions can be observed to find the effect of substituent in alkyl halide formation reaction using PBr_3 and $SOCl_2$.



$$\%\ \text{Atom Economy} = \frac{275.15}{212.25 + 270.69} \times 100\% = 57\%$$

Scheme 8:Atom economy Calculation for Bromination Reaction of Secondary Alcohol



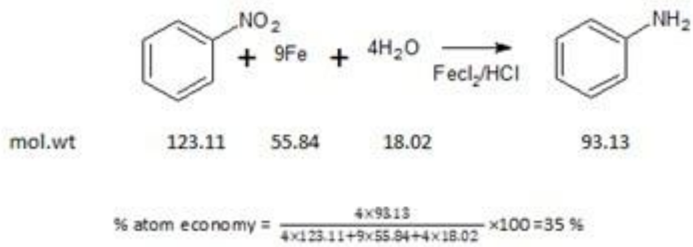
$$\%\ \text{Atom Economy} = \frac{230.69}{212.25 + 118.96} \times 100\% = 70\%$$

Scheme 9:Atom economy Calculation for Chlorination of Secondary Alcohol using Sulfonyl chloride.

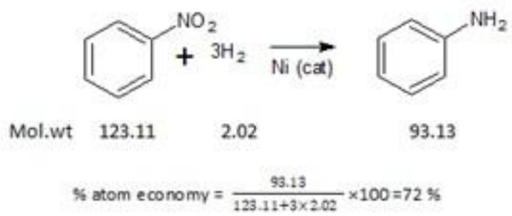
Role of catalyst in performing Atom efficient reactions :
Considering a chemical reaction involving a catalyst, where it is always used in place of a stoichiometric reagent, So its effect on atom economy can be neutral where the alternative reagent can reduce the atom economy, thus catalytic methods offer better atom efficiencies than alternative non-catalytic. In another way, as the catalytic quantities are very low, there will be less mass input into the process, which increases ratio of atom economy calculation. With the use of homogenous, heterogeneous and biocatalysts it is possible to reduce experimental constraints such as extra synthetic steps, stoichiometric components and energyinputs along with efficiency in atom economy.

HETEROGENOUS CATALYSIS:
The reactions where both catalyst and reactants are in two different phases and process occurs by adsorption of reactant molecules onto surface of catalyst. The best example is nickel catalyzed hydrogenation of nitrobenzene to accommodate global demand for aniline; nickel was picked up as cheap, easily available and recoverable catalyst with an atom efficiency of 72% whereoriginal process has only 35% economy.

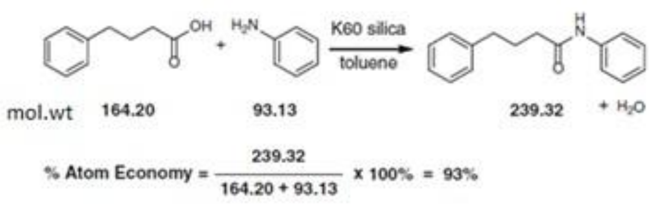
Another promising approach is the emerging use of thermally activated k60 silica as a readily available and affordable catalystfor amide bond formation in order to eliminate the use of inefficient reagents like carbodiimides, phosphonium or uranium salts etc.



Scheme 10.Atom economy Calculation for Traditional synthesis of Aniline.



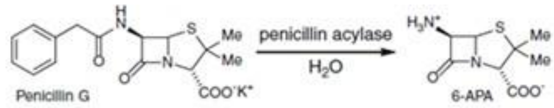
Scheme 11. Atom economy Calculation for Nickel Catalysed Aniline Synthesis.



Scheme 12.Atom economy Calculation for Catalytic Synthesis of 4-N-Diphenylacetamide.

BIOCATALYSIS: Enzymes promote chemical reactions which have numerous green chemistry advantages like biodegradability, safety, high selectivity etc. In terms of atom economy, synthesis of 6amino penicillanic acid from penicillin G highlights power of biocatalysts.

Sheldon et..at in 2001 explained the development of biocatalytic process for synthesis of 6Amino pencillinic acid using stable penicillin G acylase enzyme resulting in dramatic reduction of wastes and with milder reaction condition compared to the traditional 4 step deacylation of penicillin G to give 6APA which accounts just an atom economy of 28%.



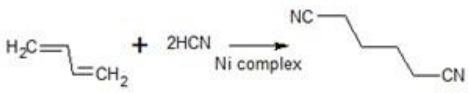
mol.wt 372.48 216.26

$$\% \text{ Atom Economy} = \frac{216.26}{372.48} \times 100\% = 58\%$$

Scheme 13: Atom economy Calculation for Penicillin acylase mediated synthesis of 6 amino penicillanic acid.

HOMOGENOUS CATALYSIS: As distinguished from heterogeneous catalysis, here the reactants and catalysts are foundto be in same phase.

Ex: In 1970 DuPont Adiponitrile Synthesis catalyzed by nickel tetrakis phosphate complex as an example of major



Mol.wt 54.09 27.03 108.14

$$\%\text{atom economy} = \frac{108.14}{54.09+2\times 27.03} \times 100 = 100\%.$$

Scheme 14:Synthesi of Adiponitrile Mediated by Nickel catalyst.

industrial process involving homogenous catalysis occurring with 100%AE.LIMITATION : In some instances, atom Economy is limited in process efficiency when the reaction can proceed with high atomeconomy but having yield of less than 50%.ex: synthesis of 2,4 diphenylquinoline where AE=93% and yield is less than or equalto50%. Here, Reaction Mass Efficiency produces robust and global perspective of greenness in such cases.
Relationship.

REACTION MASS EFFICIENCY:

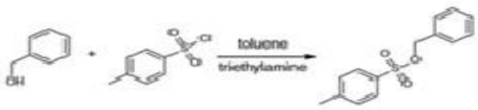
Steinbach and Winkenbach introduced the term balanced yield which is synonymous to present term Reaction MassEfficiency, and which is the measure of productivity rather than wastes generated.

Balance yield Main product amount Balance sheet total input

In 2001, GSK presented their list of green metrics to promote sustainable development among them RME was emphasized as realistic metric for greenness of reaction.

An excess of either of reactants to maximize the selectivity or yield of reaction are not included in atom economy But, in reaction mass efficiency equation which was put forth by curzos eventually recognized Reaction mass efficiency accounts for Yield ,Atomeconomy and stoichiometry factor. Following generic reaction is taken to derive such relationship

Example: By applying the derived equation following reaction of esterification of benzyl alcohol and p-toulene sulfonyl chloride.



MASS	10.81	21.9	23.6g
MOLES	0.10	0.115	0.09
GMW	108.14	190.64	262.32g

$$RME = \frac{23.6}{10.81 + 21.9} = 0.72 \qquad YIELD = \frac{0.09}{0.10} = 0.90$$

$$ATOM\ ECONOMY = \frac{262.32}{190.64 + 108.14} = 0.88$$

$$STOICHIOMETRIC\ FACTOR = 1 + \frac{(0.115 - 0.10) \times 190.64}{0.10 \times (108.14 + 190.64)} = 1.10$$

$$RME = YIELD.ATOM\ ECONOMY.1/STOICHIOMETRIC\ FACTOR = 0.90 \times 0.88 \times \frac{1}{1.10} = 0.72$$

Scheme 15Reaction mass efficiency Calculation for esterification reaction of benzyl alcohol.

Note: Results are expressed in absolute form ranging between (0-1), to make RME values meaningful as percent values cannotachieve this.

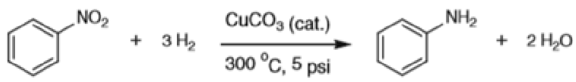
Through his work on Green metrics in 2005, Andros recognized RME to be accounted for all the materials involved in chemical process and thus proposed a generalized mass efficiency equation which can be broken down into product of yield, atom economy,stoichiometric factor and (material recovery parameters) ie; accounts for solvents, catalysts, workup /purification materials**.**

Here the Kernel RME is equal to Curzos as excess reagents are not used, but when mass of remaining reagents are used RME isdecreased as the solvents occupy 98% of mass involved in experiment.

APPLYING REACTION MASS EFFICIENCY TO CATALYSIS:
Apart of always being atom efficient, few catalytic reactions have shown that atom economy is limited at its ability to measure process efficiency. Ex: Synthesis of 2,4diphenylquinoline have shown 93% atom economy with an yield of less than 50% thus attaining less in terms of achieving reaction efficiency and productivity. Applying reaction mass efficiency metric to catalytic reactions have gained more global perspective on greenness.

HETEROGENOUS CATALYSIS:
Ex: Among 5 industrial routes in converting benzene to aniline, efficient process includes Nitration via electrophilic substitution reaction and hydrogenation catalyzed by copper carbonate on silica.RME calculations for industrial production of aniline are as follows: Here in this reaction generalized RME is much greater than Suzuki reaction representing as industrial process should bemuch more efficient than laboratory preparations.

Mass	589.7Kg	480.8kg	907.2 kg
GMW	78.11	63.01	123.11



Mass	907.2 kg	43.6kg	671.3kg
GMW	123.11	6.05	93.13

Catalytic mass -5.03 kg

Workup and purification material mass – 9.1 kg

Reaction solvent mass – 753 kg

$$\text{Generalized RME} = \frac{671.3}{589.7+480.8+43.6+5.03+753+9.1} = 0.357$$

scheme17: reaction mass efficiency calculation for catalytic synthesis of aniline.

GLUTARYL 7ACA ACYLASE
→―――――――――――――――→
SCHEME18: Conversion of potassium salt of cephalosporin C to 7ACA mediated by biocatalysts.

Where as, Biocatalytic route had given 90 fold reduction in overall waste and seven fold reduction in solvent emissions. Cephalosporin C salt is stirred with immobilized DAO and reacted with oxygen gas to produce keto intermediate. This react spontaneously to produce glutaryl 7 ACA .further, Enzyme is again recycled and reaction is stirred with glutaryl 7-ACA acylase to form 7 Aminocephalosporonic acid. NOTE: RME Values less than 0.15 are unproductive and less efficient. As, this metric accounts for most of all reactant masses and also as it is a combined metric of atom economy, yield and stoichiometic factor ,it can be considered To be a helpful greennessmeasurement.

CONCLUSION

Green chemistry is been considered as added value to organic chemistry. Greenness assessment tools that can well assess e-impact of chemical process and reaction efficiencies are to well understand before going through a chemical synthesis. Assessment of greenness with large input datasets have to be made by developing more efficient metrics.Atom economy is one way to measure the idealness of said synthesis. New software and tools are expected to be developed for easy calculations of standards and also there is a need for popularization of existing metrics. Atom economy even cannot be considered as a stand-alone metric, can be used as organizing concept and in combination withother metrics.

Yield can remain as ubiquitous metric in economic standpoint and for high value added materials like in pharmaceuticals. RME combines most of key properties of process and chemistry and represents a simple, objective and a well derived metric and it drives for invention of likely chemical process and technologies that lead to more sustainable development.

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