WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 8, 508-515. Review Article ISSN 2277– 7105

PHASE TRANSFER CATALYST IN ORGANIC SYNTHESIS

Dirgha Raj Joshi[1]* and Nisha Adhikari[2]

[1]College of Pharmacy, Yonsei University, 85 Songdogwahak-ro, Yeonsu-gu, Incheon 21983, Republic of Korea.

[2]College of Pharmacy, Wonkwang University, Republic of Korea.

Article Received on
08 May 2019,

Revised on 29 May 2019,
Accepted on 20 June 2019

DOI: 10.20959/wjpps20198-15348

***Corresponding Author**
Dirgha Raj Joshi
College of Pharmacy, Yonsei University, 85 Songdogwahak-ro, Yeonsu-gu, Incheon 21983, Republic of Korea.
ORCID ID: 0000-0002-0303-5677
djmeropaila121@korea.ac.kr,
djmeropaila121@gmail.com

ABSTRACT

Phase-transfer catalyst (PTC) has been popular for more than four decades in synthetic chemistry. The PT catalysis uses the PTC in a catalytic amount and it allows to react the reactants of two different phases via facilitating transfer of reactants from interface, which are not miscible and itself regenerated again and the cycle is repeated. The use of PTC is wide from liquid-liquid, solid-liquid to liquid-gas system. Due to its diversified application, PTC is also combined with other rate enhancing techniques like microwave, electro-organic synthesis, sono-chemistry, photochemistry and many more are exploring. The PTC application in the field of manufacturing of the fine chemicals and organic intermediates are unlimited.

KEYWORDS: Phase-transfer catalyst, organic reaction, catalyst, catalysis, reaction, ammonium salt, phosphonium salt.

INTRODUCTION

The catalyst is an agent used to enhance the rate of chemical reaction which itself not consumed throughout the reaction process and act continuously which is the rational of using it in a very small amount.[1] It usually works by lowering the activation energy or altering the mechanism of reaction. In biological system, the enzyme acts as a catalyst.[2] The catalysis is a term used to describe the role of catalyst.[3-5]

PTC has been introduced in around 1965 and within a decade, it became popular in synthetic organic chemistry.[6] Many researches with employing PTC are published. The phase transfer catalyst (PTC) is that which allows exchanging of the chemical reactions between the two non-miscible, heterogeneous systems. PTC itself has both functional sites to get solubilized in

both system and allow transferring substance from one system to another.[6] It is usually a salt of quaternary ammonium, phosphonium compound and crown ether etc.[7] So PTC is usually used in a heterogeneous reaction system where it facilitates migration of reactant from one phase to another.[8] Since it accelerates the reaction, decreases reaction time, needs less solvents, obtains higher yield, has less side reaction, and eliminate hazardous waste etc, so regarded as good agent for Green Chemistry which allows reaction in water and the use of organic solvents is dramatically decreased.[9] The reactants with ionic nature are soluble in aqueous system but insoluble in organic medium so to make the reaction happen, the PTC is used which acts like a detergent to solubilize the salt in to the desired organic medium. Normally, the reaction with PTC can be carried out in mild conditions and easy workup procedure so highly used in industrial scale.[10] With contrary to the general understanding, PTC is not limited to hydrophilic and lipophilic system but in some cases it is highly useful and utilized in liquid/gas and liquid/solid reaction conditions.[6] Generally, the PTC can be categorized as below and the examples are listed in chart which are compiled from the commercial sources like Sigma Aldrich[11], TCI[12] and other.

Ammonium Salts

These are the chemical compounds having nitrogen in their skeleton and formed a salt with different structural nature.[8,13] The chart 1 shows the commonly used ammonium salt category PTC.

Heterocyclic Ammonium Salts

These are similar to the ammonium salt but only difference is that there is one or more hetero atom in their structure.[14] The chart 2 shows the commonly used heterocyclic ammonium salt category PTC.

Phosphonium Salts

These are also similar to the ammonium salt but instead of nitrogen, it contains phosphorous.[8,15-17] The chart 3 shows the commonly used phosphonium category PTC.

Nonionic PTC

These are less common and less in number. They don't contain charge on their structure. But for some specific reaction, it's popularity is also increasing.[18,19] The one listed by Sigma Aldrich is DL-α-Tocopherol methoxypolyethylene glycol succinate[11] and other are also commercially available.

Crown ether as PTC

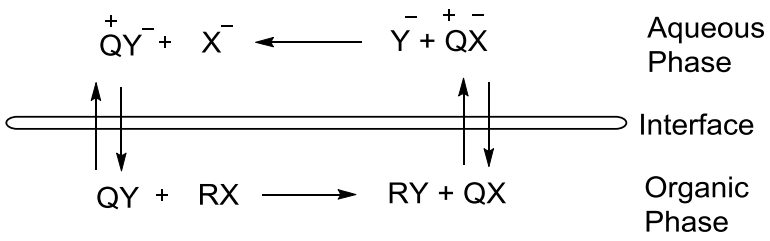
Many commercially available crown ether can be found easily[20] and are employed as a PTC in various kinds of reactions.[21-24] The role of crown ether as PTC in polymer science are also diversely studied.[25] Few of the crown ether are listed in chart 4.

Principle of PTC

The general principle can be discussed as the ability of PTC to facilitate transfer of the reagent from one phase (eg. Hydrophilic) to another phase (eg. Lipophilic) which are immiscible and it is regenerated to its original state so the amount of PTC is in catalytic amount.[6,7,10,26,27] So those reactions are also possible which are originally not in contact with each other due to their insolubility in two different phases.

Mechanism of PTC reaction

In 1971 the mechanism of PTC reaction was proposed by Starksi original research where a quaternary ammonium halide undergoes dissolution in aqueous phase (Q+X-) and anion exchanges with another anion from the reactants dissolved in aqueous phase. The formed ion pair (Q+X-) now can pass through liquid-liquid interface because of its lipophilic nature and undergoes diffusion from interface to the lipophilic phase, this key step is the phase transfer. In the lipophilic phase, the anion from ion pair is nucleophilic which undergoes reaction (nucleophilic substitution) with the organic reagents and forms subsequent desired product (RY). Again the catalyst after its work is done, returns back to the aqueous phase and the cycle is repeated continuously.[8] The overview of PTC reaction is explored in below Scheme 1.



Scheme 1. Overview of PTC reaction

Application of PTC: More new and new applications are reviling with PTC. Usually it plays a great role in Green chemistry to minimize waste, use of less solvent, faster and convenient approach etc. In organic synthesis also, various reactions are catalyzed by PTC usually where the reagents form heterogeneous nature in a reaction medium. So the PTC is now employed

industrially. Like the polyester polymer are made from bisphenol-A and acid chloride, the PTC catalyzed pesticide production are popular usually via alkylation of phosphothioates. The asymmetric[28,29] alkylation is another advance application of PTC where the chiral quaternary ammonium salt is employed which are derived from cinchona alkaloids.

PTC in Green Chemistry: The general catalyst has great role in green chemistry to perform reaction conveniently, good yield, less hazardous byproducts and many more.[9] Specially, the use of PTC is also increasing which directly enhance the less use of organic solvents, so ultimately less hazardous byproducts and other organic solvents related problems. The wide application of PTC in aqueous system allow more enhanced environment friendly green synthesis. Solvent free synthesis is also possible using PTC.[30,31]

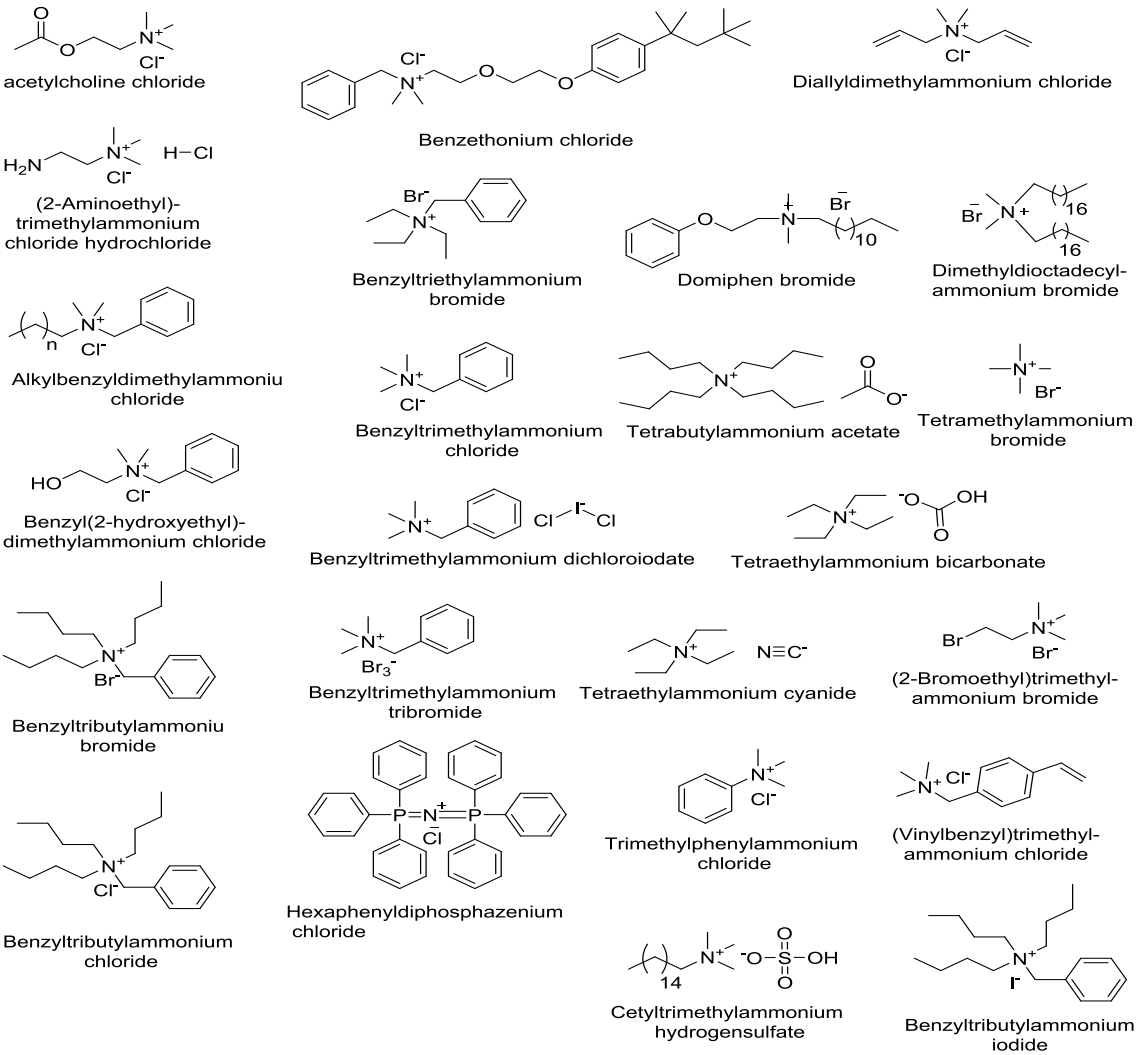
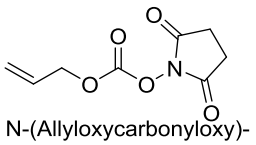
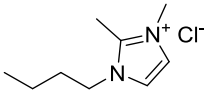
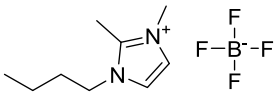
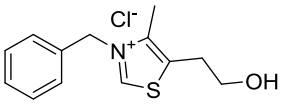


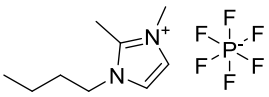
Chart 1. Ammonium Salts

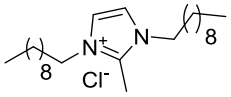

N-(Allyloxycarbonyloxy)-succinimide

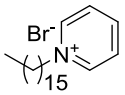

1-Butyl-2,3-dimethylimidazolium chloride

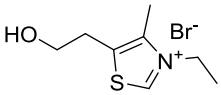

1-Butyl-2,3-dimethylimidazolium tetrafluoroborate


3-Benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride


1-Butyl-2,3-dimethylimidazolium hexafluorophosphate


1,3-Didecyl-2-methylimidazolium chloride


Hexadecylpyridinim bromide


3-Ethyl-5-(2-hydroxyethyl)-4-methylthiazolium bromide

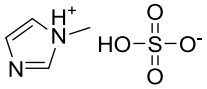
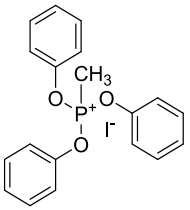
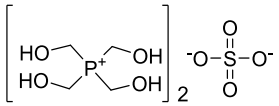
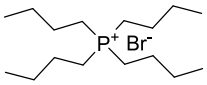
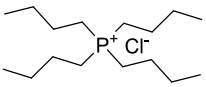

1-Methylimidazolium hydrogen sulfate

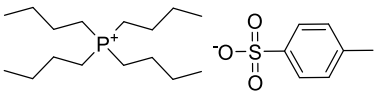
Chart 2. Heterocyclic Ammonium Salts

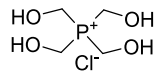

Methyltriphenoxy-phosphonium iodide

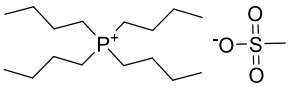

Bis[tetrakis(hydroxymethyl)-phosphonium] sulfate

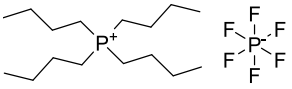

Tetrabutylphosphonium bromide

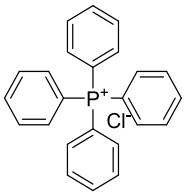

Tetrabutylphosphonium chloride

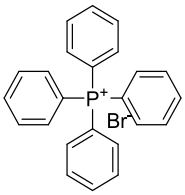

Tetrabutylphosphonium p-toluenesulfonate

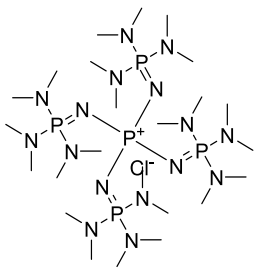

Tetrakis(hydroxymethyl)-phosphonium chloride

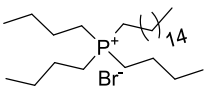

Tetrabutylphosphonium methanesulfonate


Tetrabutylphosphonium hexafluorophosphate


Tetraphenylphosphonium chloride

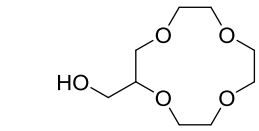

Tetraphenylphosphonium bromide


Tetrakis[tris(dimethylamino)-phosphoranylidenamino]-phosphonium chloride

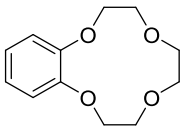

Tributylhexadecylphosphonium bromide


Tetramethylphosphonium chloride

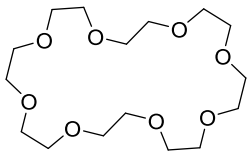
Chart 3. Phosphonium Salts



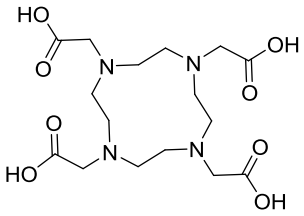
2-(Hydroxymethyl)-12-crown 4-Ether



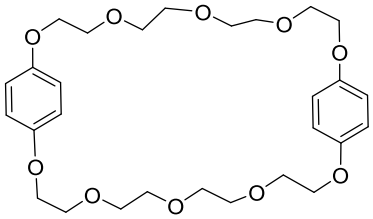
Benzo-12-crown 4-Ether



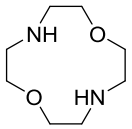
24-Crown 8-Ether



1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic Acid



Bis(1,4-phenylene)-34-crown 10-Ether



4,10-Diaza-12-crown 4-Ether

Chart 4. Crown Ether

CONCLUSION

From past 4 decades, the PTC popularity is increasing and many significant reactions are performed as desired with employing PTC. Only in a commercial scale the disadvantage is that, we need to separate PTC from the product containing organic phase. Nowadays more diversified chemical structure with ammonium, phosphonium, crown and the nonionic PTC are developed and available commercially which allows us to select the specificity to the certain reaction nature. Moreover, the chiral PTC are playing great role in asymmetric synthesis. So we hope this concise review will provide information regarding PTC with most commonly used/ available PTC reagents in one place.

ACKNOWLEDGEMENT

We heartily acknowledge Yonsei University, College of Pharmacy and Wonkwang University, College of Pharmacy for providing space and needed things to prepare this manuscript.

REFERENCES

1. Twigg, M.V., Catalyst handbook. 2018: Routledge.
2. ES, E., Enzyme kinetics, 1975.
3. Jencks, W.P., Catalysis in chemistry and enzymology. 1987: Courier Corporation.
4. Romero, N.A. and D.A. Nicewicz, Organic photoredox catalysis. Chemical reviews, 2016; 116(17): 10075-10166.
5. Hagen, J., Industrial catalysis: a practical approach. 2015: John Wiley & Sons.

6. Starks, C.M. and M. Halper, Phase-transfer catalysis: fundamentals, applications, and industrial perspectives. 2012: Springer Science & Business Media.
7. Sasson, Y. and R. Neumann, Handbook of phase transfer catalysis. 2012: Springer Science & Business Media.
8. Starks, C.M., Phase-transfer catalysis. I. Heterogeneous reactions involving anion transfer by quaternary ammonium and phosphonium salts. Journal of the American Chemical Society, 1971; 93(1): 195-199.
9. Rothenberg, G., Catalysis: concepts and green applications. 2017: John Wiley & Sons.
10. Reuben, B. and K. Sjoberg, Phase-transfer catalysis in industry. Chemtech, 1981; 11(5): 315-320.
11. https://www.sigmaaldrich.com/chemistry/chemistry products.html?TablePage=16278277.
12. https://www.tcichemicals.com/eshop/en/be/category_index/12692/.
13. Lygo, B. and B.I. Andrews, Asymmetric phase-transfer catalysis utilizing chiral quaternary ammonium salts: asymmetric alkylation of glycine imines. Accounts of chemical research, 2004; 37(8): 518-525.
14. Verbicky Jr, J.W. and A.M. Colley, Heterocyclic quaternary ammonium salts as phase transfer catalysts for aromatic ether imide preparation, 1986, Google Patents.
15. Molinari, H., et al., Polymer-supported phase-transfer catalysts. High catalytic activity of ammonium and phosphonium quaternary salts bonded to a polystyrene matrix. Journal of the American Chemical Society, 1979; 101(14): 3920-3927.
16. Cao, D., et al., Thiourea-phosphonium salts from amino acids: cooperative phase-transfer catalysts in the enantioselective aza-Henry reaction. Chemical Communications, 2013; 49(53): 5972-5974.
17. Tomoi, M., et al., Phase-transfer reactions catalyzed by phosphonium salts attached to polystyrene resins by spacer chains. Journal of Polymer Science: Polymer Chemistry Edition, 1982; 20(12): 3421-3429.
18. Pogrzeba, T., et al., Understanding the role of nonionic surfactants during catalysis in microemulsion systems on the example of rhodium-catalyzed hydroformylation. Industrial & Engineering Chemistry Research, 2017; 56(36): 9934-9941.
19. Berglund, K.D., et al., Use of nonionic ethylene oxide surfactants as phase-transfer catalysts for poly (acrylic acid) adsorption to silica against an electrostatic repulsion, in Aqueous Polymer—Cosolute Systems. 2003; 56-66.
20. https://www.tcichemicals.com/eshop/en/be/category_index/12953/.

21. Landini, D., et al., Crown ethers as phase-transfer catalysts. A comparison of anionic activation in aqueous–organic two-phase systems and in low polarity anhydrous solutions by perhydrodibenzo-18-crown-6, lipophilic quaternary salts, and cryptands. Journal of the Chemical Society, Perkin Transactions 2, 1980; (1): 46-51.
22. Childs, M.E. and W.P. Weber, Preparation of cyanoformates. Crown ether phase transfer catalysis. The Journal of Organic Chemistry, 1976; 41(21): 3486-3487.
23. Landini, D., F. Montanari, and F.M. Pirisi, Crown ethers as phase-transfer catalysts in two-phase reactions. Journal of the Chemical Society, Chemical Communications, 1974; (21): 879-880.
24. Herriott, A.W. and D. Picker, Phase transfer catalysis. Evaluation of catalysis. Journal of the American chemical Society, 1975; 97(9): 2345-2349.
25. Mathias, L.J. and C.E. Carraher, Crown ethers and phase transfer catalysis in polymer science. Vol. 227. 1984: Springer.
26. Weber, W.P. and G.W. Gokel, Phase transfer catalysis in organic synthesis, 4. 2012: Springer Science & Business Media.
27. Naik, S.D. and L. Doraiswamy, Phase transfer catalysis: chemistry and engineering. AIChE Journal, 1998; 44(3): 612-646.
28. Maruoka, K., Asymmetric phase transfer catalysis. 2008: John Wiley & Sons.
29. Ooi, T. and K. Maruoka, Recent advances in asymmetric phase-transfer catalysis. Angewandte Chemie International Edition, 2007; 46(23): 4222-4266.
30. MOBINIKHALEDI, A., et al., Solvent Free Synthesis of Pyrimidine, Quinazolinone and Diazatricyclo Derivatives via Phase-Transfer Catalysis Method (PTC). Chemical Science, 2015; 4(4): 1066-1070.
31. Albini, A. and S. Protti, Activation of Chemical Substrates in Green Chemistry, in Paradigms in Green Chemistry and Technology. 2016, Springer. p. 25-61.