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List of phase transfer catalyst

However, the quaternary salts, with chains from 5 to 8 carbon atoms, even if they remain for about 95% in the organic phase, give the highest conversions of the overall process. Journal of the Chemical Society, 21, 879. The micelle distributes itself into the organic phase, effectively transferring the anion with its water molecules. More importantly, PTC can allow the use of a wider range of solvents other than dipolar aprotics. 626-638. Liotta, M. In fact, it is very probable that if a homogeneous phase reaction is slow, the same will be with phase transfer catalysis. Thus, NaCl is formed in the aqueous phase. Sometimes a few drops of water are sufficient for the transfer or even the hydration water of the inorganic salt is enough. Salts with excessively long chains, completely insoluble in water, however, fail to properly interact at the interface and the reaction is rate-limited by phase transfer. This mechanism can easily be remembered by thinking of Q+ as a shuttle service that transports an anion from the aqueous phase to the organic phase, activates it for the reaction and carries the replaced anion back to the aqueous phase. The rate of agitation is very important in phase transfer reactions because increased agitation generally results in an increase in the anion transfer rate. In PTC, the use of high concentrations of inorganic salts in the aqueous phase favours phase transfer, because the quantity of the anion will be greater and therefore the catalyst will be able to bind and transfer it more easily. Only at this point, the phase transfer catalyst (Q+) steps in, transporting the anion from the interface into the internal part of the organic phase, where the reaction between the anion and the electrophile (EX) takes place. Attribution — You must give appropriate credit , provide a link to the license, and indicate if changes were made . No warranties are given. Thus, the C# for methyl tributyl ammonium is 1 + 4 + 4 + 4 = 13. pp. In particular, four situations can occur, described by the graph in Figure 3: The intrinsic reaction rate is high, but phase transfer is slow (upper left quadrant). Starks[1] demonstrated how this reaction could be carried out in a heterogeneous phase, but with the condition to add a quaternary ammonium or phosphonium salt soluble in the organic phase. Using the mesylate gave 95% yield whereas using the tosylate gave 5% yield! These are both good leaving groups, however the quat pairs more strongly with tosylate than mesylate which in turn hinders the ability of the quat to transfer and react the desired nucleophilic anion. Phase-Transfer Catalysis: Fundamentals, Applications, and Industrial Perspectives. Phase transfer catalysis is a technique for carrying out reactions between two or more reactants, which are in two or more different phases, thanks to the use of a phase transfer agent. (2011). M. The mechanism of the reaction occurs with the crown ether bringing both the cation and the anion into the organic phase (Scheme 7). In organic solution, the CN– ion, which is now even more reactive, reacts with R-Cl to give R-CN. Int. Therefore, in the case of a slow transfer, increasing the stir of the reaction can help; however, this strategy will have no effect on the intrinsic rate of reaction. Less water also helps to have less hydrated anion, which are more difficult to transfer due to the strong bond with water molecules. Molinari in 1974:[3] Scheme 6 - Substitution reaction with crown ether Dicyclohexyl-18-crown-6 catalyzed the substitution reaction of methanesulfonate with CN– in 90% yield in a short time. V. In addition, the counterion of the anion to be transferred plays an important role in the solubility of the anion itself. Finally, the first examples of PTC for transferring cations via anionic catalysts have also recently appeared.[2] In this short article, we will mainly cover the transfer of anions through quaternary ammonium and phosphonium salts; however, there will be references, where appropriate, to the transfer by neutral catalysts. Let’s use again the reaction of cyanide with 1-chlorooctan as an example of a simple transfer. Asymmetric Electrophilic Fluorination Using an Anionic Chiral Phase-Transfer Catalyst. This is the worst scenario because both processes will need to be tuned up. 2008, 12 , 679–697 Practical Aspects of Recent Asymmetric Phase-Transfer Catalysis Angew. For example, in the case of the substitution reaction of 1-chlorooctane with NaCN, high concentrations of NaCN or even its use as a solid favour the formation of the Q+CN– bond and make the bond between Q+Cl–, which involves the leaving group, less competitive in the aqueous phase. Therefore, phase transfer catalysis works through a double action: transfer of a reactant and its activation. No additional restrictions — You may not apply legal terms or technological measures that legally restrict others from doing anything the license permits. Widely studied in this regard was the reaction between 1-chlorooctane (in decane) and sodium cyanide in water (Scheme 1). Therefore, the use of saturated concentrations of the anion are advisable to increase the phase transfer. Regarding the speed of the transfer, one can get an idea of the performance of the anion during the transfer, by consulting the literature on phase transfer catalysis involving the same anion. Phase-transfer catalysis. As the C# increases, the organophilicity increases and usually results in a higher concentration of the quat-anion pair in the organic phase. S., & Toste, F. Dichloromethane is a solvent polar enough to solubilize most quaternary salt catalysts and to speed both phase transfer and the intrinsic reaction. Not all anions transfer quickly. While the slowest ions to transfer are OH–, F–, ClO–. Ultrasound can also be used as an agitation tool to enhance anion transfer. 2011, 15, 817–823 Phase Transfer Catalyzed Wittig Reaction in the Microtube Reactor Relevant scale up example Experimental Cyclohexane/ H2O/ NaOH/ nBu4NCl 25 Kg scale Org. S. The counter ion of the electrophile (X–) is brought to the interface by the catalyst and then goes into the aqueous phase together with the M+ cation coming from the base. Thus, the q-value for methyl tributyl ammonium is 1/1 + 1/4 + 1/4 + 1/4 = 1.75. However, it is necessary that the transferred species is also activated towards the reaction so that only catalytic amounts of the phase transfer agent can be used. Both speeds are high (upper right quadrant); it is good here to pay attention that the process does not become uncontrollable; Both reactions are slow (lower left quadrant). The following table summarizes the parameters to change in order to improve the rate in PTC reactions according to the starting situation (reaction limited by transfer, fast overall reaction, slow overall reaction and reaction limited by reaction in organic phase). 2007, 11, 754-761 Share — copy and redistribute the material in any medium or format for any purpose, even commercially. Anions such as MnO4–, ClO4–, I– are known for their high transfer rate. The license may not give you all of the permissions necessary for your intended use. This anion is both difficult to transfer into the organic phase and is a weak nucleophile. Scheme 2- Reaction with phase transfer catalysisWould you like to print this article or save it on your computer and read it offline ? (1971). Phase transfer catalysts are not only cationic, but can also be neutral molecules such as crown ethers, cryptands, polyethylene glycol (PEG) etc. At first glance, the reaction would be impossible since the reagents, being in different phases, could not come into contact with each other and therefore react. Scheme 1 - Substitution reaction in homogeneous phase In 1971, the chemist Charles M. Starks, C. The use of even longer alkyl chains on the quaternary salts involves a loss of the catalyst activity: the catalyst will be almost exclusively soluble in the organic phase, losing the ability to partition in the aqueous phase and therefore to carry out the transfer of the anion The second mechanism involves anion exchange at the interface between the two phases. Catalysts such as crown ethers and PEGs can carry out the transfer of the inorganic compound even starting from the solid in the absence of water. D. Scheme 4- Simple transfer through the interface Quaternary salts with long alkyl chains such as tetrahexyl and tetraoctyl exhibit this type of mechanism, as they are mainly partitioned in the organic phase (99%), but can interact at the interface. 400-410; Industrial considerations, pp. ShareAlike — If you remix, transform, or build upon the material, you must distribute your contributions under the same license as the original. Excellent summary of C-N bond forming reactions prior to 1992 General Phase Transfer Catalysis C-N bond formation references Org. In this case, the mechanism is different from those seen above. Adapt — remix, transform, and build upon the material for any purpose, even commercially. Science, 334(6063), 1681–1684. Temperature generally accelerates reactions and so does in PTC, however the catalyst may decompose at certain temperatures. Intermediate speeds result from ions such as Cl–, Br–, NO3–, CN–, NO2–. G. Figure 1- Ionic bond lenghts The increased distance in Q+Br- makes the Br- anion more naked and therefore more reactive towards the electrophile in the organic phase. Figure 2 - Inverse micelles When the catalyst is soluble neither in aqueous phase nor in organic phase, it form a third phase. Chem. Let’s see below what these parameters are and how to use them. I. Halpern, “Process Chemistry in the Pharmaceutical Industry,” K. The application of PTC can allow very concentrated or neat reactions if reagents are liquids. Goldberg, “Phase Transfer Catalysis” Gordon and Breach Science Publishers, 1992. Key references Books E. Scheme 7 – Mechanism of Catalysis with macrocyclei In phase transfer reactions the rate of the entire process is actually composed of two rates: The rate of the reaction in the organic phase, called the intrinsic rate; The speed of phase transfer. (1982). 147–206). 3) Landini, D., Montanari, F., & Pirisi, F. 1) Starks, C. This agent takes care of transferring a chemical species into the phase where the other reagent is present. Phase Transfer Assisted Permanganate Oxidations. Process Res. PTC is scalable and readily carried out at industrial scale Greenness Phase Transfer Catalysis offers the greenest variant of the SN2 reaction Use of more benign solvents (toluene, MTBE) instead of dipolar aprotic solvents Higher productivity- many examples have been carried out under solvent-free conditions Use of inorganic bases (NaOH, carbonate) instead of bulky organic bases (diisopropylethylamine, DBU, lithium hexamethyldisilazide, etc.) General comments The "q-value" and "C#" are two empirical parameters which are used to characterize the structure of quaternary ammonium salts for structure-activity relationships. At this point the reaction can take place. In such a situation, the anion is at a great distance from its counter ion and will be able to react even faster in the substitution reaction, being a naked ion. In this case, the mechanism involves the passage of reactants directly in the catalyst phase where their reaction occurs. In this case, the quaternary salt does not go into aqueous solution but is limited to carrying out the transfer at the interface (Scheme 4). This is because there are too many water molecules strongly bound to the anion, the anion cannot detach from them and is blocked in the aqueous phase. The use of microwaves in PTC has generally resulted in an increase in the speed of the overall process. (1994). As mentioned above, the phase transfer catalyst in addition to transferring the anion also activates it. C# is simply the total number of carbons on the 4 alkyl chains. The licensor cannot revoke these freedoms as long as you follow the license terms. In this case, it is necessary to intervene on the parameters that influence the reaction in the organic phase. 4) Lee, D. Most phase-transfer reactions involve the transfer of an anion, because the organic reactions themselves mostly occur via anions; in this case the transfer is mainly performed by quaternary salts. Dev. In this case we should try to improve the phase transfer; Phase transfer is fast, but intrinsic velocity is slow (lower right quadrant). Another activation mechanism is the fact that the transfer of the anion into the organic phase via the catalyst involves less water of hydration around the anion, making the latter more naked and therefore more reactive. To understand whether the reaction in the organic phase will be fast or slow, the reaction in question can be compared with the one performed in the homogeneous phase using the data available in the literature. This is because agitation increases the interfacial contact area between the aqueous and organic phases, allowing the anion to be transferred. The reason for this effect is due to the ability of the microwave to interact especially with water, removing the hydration molecules from the anion, which become more reactive. For example, other rights such as publicity, privacy, or moral rights may limit how you use the material. A solvent in which the catalyst is insoluble can also be chosen to favour the formation of a third phase. Phase transfer catalysis (PTC) is a very useful technique to employ in the synthesis of amines via SN2 alkylation PTC often allows the use of weaker, more environmentally friendly inorganic bases compared to organic and organometallic bases. The "q-value" parameter is often useful when the rate determining step is mass transfer ("T-reaction"), especially when using hydrophilic anions such as hydroxide (about half of PTC applications fall in this category). The q-value is calculated by adding the reciprocals of the number of carbons on each of the four chains of the quat. Moreover, the insoluble catalyst can be easily removed and recovered at the end of the reaction. One way to lower the transfer barrier is the formation of reverse micelles (Figure 2), where the quaternary salt forms a micellar structure around the hydrated anion, placing the hydrophobic chains on the outside and the cationic moiety on the inside. Guideline: Consider bromide instead of iodide and mesylate instead of iodide. This mechanism occurs according to the following scheme: Scheme 3- Simple transfer As can be seen, the CN– ion is transferred from the aqueous solution to the organic solution by the quaternary ammonium or phosphonium salt (Q+). 283-296 Y. Journal of the American Chemical Society, 93(1), 195–199. In fact, by conducting the reaction with 5% hexadecyltributylphosphonium bromide, 99% yield of cyanooctane was obtained after only 1.8 hours (Scheme 2). Scheme 5- Mechanism of anion formation at the interfacial area without catalyst Highly hydrated ions, such as dilute solutions of sodium hydroxide, fluoride and sulfate, make the usual simple transfer or interface mechanism impossible and follow a reverse micelle mechanism. 25-91 and 101-126 for C-N bond discussion. (1974). L., & Halpern, M. Quaternary ammonium phase-transfer catalysts sometimes experience "poisoning" by highly polarizable or lipophilic leaving groups, most notably iodide and tosylate. Ed. 2007, 46, 4222–4266 Recent Advances in Asymmetric Phase-Transfer Catalysis Topics in Catalysis 2004, 29, 145-161 Insight into Green Phase Transfer Catalysis AIChE 1998, 44, 612-646 Phase Transfer Catalysis: Chemistry and Engineering Org. Crown ethers as phase-transfer catalysts in two-phase reactions. Ed. 2013, 52, 4312–4348 Recent Developments in Asymmtric Phase Transfer Reactions Org. Consequently, the organic reagent can penetrate into the micelle through the organophilic region of the quaternary salt chains. In Organic chemistry (pp. You may do so in any reasonable manner, but not in any way that suggests the licensor endorses you or your use. The phase transfer catalyst can influence both the transfer rate and the rate of the intrinsic reaction and this mainly depends on its structure: A quaternary salt with too short alkyl chains (e.g. (CH3)4N+) is not able to partition well in the organic phase and hence greatly limits the speed of phase transfer; A quaternary salt with enough long chains (e.g. tetrahexyl- or trioctyl-methylammonium salts) can partition well between the organic phase and the aqueous phase facilitating the phase transfer; Very bulky catalysts (e.g. tetrahexyl ammonium salts) are good for intrinsically slow reactions; in fact the anion will be less bound to the catalyst, more naked and therefore more reactive; Open-faced catalysts (e.g. hexadecyltrimethyl ammonium), i.e. very accessible on the one hand, are good for increasing phase transfer because they increase the interfacial area of interaction with the anion; If both reactions are slow, two catalysts can also be used, one that increases phase transfer and the other that activates the anion in the intrinsic reaction. At the same time, the phase transfer catalyst (Q+) binds the counter ion Cl– and brings it into the aqueous phase. M., Liotta, C. Dehmlow, “Phase Transfer Catalysis,” 3rd edition VCH Publishers, NY (1993) C. When the rate determining step is the organic phase reaction ("I-Reaction"), C#’s in the range of 16 to 32 often provide desirable reactivity. As alternative you can find also the docx file if you need to change the document. You can download the pdf file here. 2008, 12 , 698–709 – PTC in OPRD: An Illustrative Overview Angew. Depending on the type of catalyst and reagents used, various mechanisms are possible which we list below. Dehmlow, S. To plan a phase transfer reaction, it is good to first get an idea of the rate of the overall reaction. 2) Rauniyar, V., Lackner, A. This can also be done by decreasing the amount of water present. Very small quaternary salts, such as (CH3)4N+, are soluble only in the aqueous phase and therefore cannot transfer the anion to the organic phase, preventing the reaction. In one application, an alcohol was converted to a sulfonate ester for displacement. Heterogeneous reactions involving anion transfer by quaternary ammonium and phosphonium salts. Finally, after having studied the literature, it will be possible to take into account the various parameters that can influence the kinetics, bearing in mind that a single parameter can have an effect on phase transfer and an opposite effect on the intrinsic reaction rate. Gadamasetti, Ed (1999), CRC Press, p. How can I make a reagent in water react with a reagent in a water-immiscible organic solvent? Thus the study of kinetics is complicated due to the presence of two processes (the reaction and the transfer), both with their own speed. In this regard, the reaction can be thought as divided into two steps: the intrinsic reaction and the phase transfer. The base deprotonates an organic acid molecule (SH), transforming it into anion (S–). For T-reactions, quats with q-values in the range of 1 to 2 often promote desirable reactivity, with q-values of 1.5 to 1.75 often being the best. Figure 3 - Graph of the four kinetic region An example of a reaction that occurs in the “fast region” of the graph is the oxidation of organic compounds with permanganate.[4] This reaction is fast both because MnO4– is one of those anions that transfer more easily, and because it is also very reactive in the oxidation of alcohols, alkenes, aldehydes. In addition, an example of a reaction in the “slow region” is the nucleophilic substitution performed with F–. This type of catalysis is in general even faster than the phase transfer reactions in two phases. On the other hand, relatively small quaternary salts, i.e. having alkyl chains from 2 to 4 carbon atoms, are capable of being easily partitioned between the organic and aqueous phases according to the simple transfer mechanism. Conversely, if both reactions are fast, almost any catalyst will be able to carry out the reaction. However, neutral catalysts such as crown ethers, cryptands and polyethylene glycol (PEG) transfer both the anion and the cation into the organic phase. The most used solvents in PTC are dichloromethane, toluene, hexane, heptane. C-N bond formation, pp. In fact, let us consider the following reaction performed for the first time by F. Activation occurs because the bond between the catalyst and the anion has a greater distance than that of the anion and its counter ion. You do not have to comply with the license for elements of the material in the public domain or where your use is permitted by an applicable exception or limitation . Unlike other reactions, PTC offers the possibility of not using any organic solvent in case the reactants are liquid; otherwise, a solvent is necessary if the organic substances are solid at the operating temperature. However, the organic solvent has an influence above all on the intrinsic rate, because if it is polar but not protic it can activate the anion towards the reaction. Halpern, “Phase Transfer Catalysis,” Chapman and Hall, NY, (1994). For example, compare the anion-cation distances in NaBr and tetrabutylammonium bromide (Figure 1). L. Crown ethers or polyethylene glycols are resistant under basic conditions, but are sensitive under acidic ones. M. The reaction, carried out at 105°C, after two weeks produced only the hydrolysis of cyanide to sodium formate (HCOONa). In the case of some base-catalyzed reactions, the mechanism involves the presence of the base itself at the interface (e.g. OH– in Scheme 5). 5) Starks, C. E. In this case, it is advisable to evaluate the influence of each parameter on each of the two steps. For example, the use of KCN instead of NaCN favours the solubility of the salt and therefore increases the concentration of CN- ions in the aqueous phase. Cl– restores the electro-neutrality of the aqueous phase, which, having previously lost the anion CN–, had an excess of positive charges in the form of Na+. A technique of very wide utility, substrate scope extends to aliphatic nucleophiles and heterocycles. Elsevier BV. For example, quaternary ammonium salts are known to resist up to 120-150°C, but they also decompose at 50-70°C in alkaline solutions of KOH and NaOH. This was one of the first examples of phase transfer catalysis (abbreviation PTC). D., Hamilton, G.