Phase-transfer catalysis (PTC) is nowadays a well-established methodology to perform reactions using environmentally benign reagents and solvents. Reactions are carried out in a heterogeneous, mutually immiscible two-phase system, in which one phase provides anions or a base for their generation, whereas the second phase contains the organic reactant and the PT catalyst, usually a lipophilic quaternary ammonium or phosphonium salt. The reacting anion can thus be brought to the organic phase where the reaction occurs.\textsuperscript{1}

Mild reaction conditions, safety, operational simplicity, and high selectivity are widely accepted typical features of PTC processes that allow an easy scale-up of reactions. Indeed, numerous industrial applications,\textsuperscript{2} e.g., in pharmaceutical and agrochemical industry, as well as in monomer synthesis and polymer modification,\textsuperscript{3} have been developed. More than four decades have passed since the landmark paper of Starks describing PTC was published.\textsuperscript{4} Nevertheless, many new applications, both academic and industrial, show that this methodology is continuously appreciated as a valuable tool for organic synthesis. Moreover, the great development in asymmetric PTC reactions has enormously increased the synthetic potential of this methodology.\textsuperscript{5}

This microreview will focus on oxidative transformations carried out under PTC conditions. The oxidation will be considered in a broad sense. Since oxidation is defined as a chemical reaction which causes carbon to decrease electron density, reactions that break bonds between carbon atoms and less electronegative atoms (hydrogen), forming bonds with more electronegative atoms (i.e., oxygen, halogen) will be described. Therefore, not only classical oxidation reactions, but halogenations and C–H activation will also be covered.\textsuperscript{6}

This review does not intend to be exhaustive, but it will present selected subjects in order to illustrate the great potentiality of PTC in the field of oxidation.

2. OXIDATION

In spite of the paramount importance of oxidation processes in converting hydrocarbons to useful chemicals, they have been mostly exploited by using toxic metal oxidants such as the hexavalent chromium salts. Furthermore, not environmentally friendly and expensive stoichiometric organic oxidants have been employed, thus generating the desired product along with huge amounts of byproducts to be disposed of.\textsuperscript{5} The choice of the oxidant is undoubtedly the main factor that defines the sustainability of an oxidation reaction. Although molecular oxygen is an ideal oxidant, it also often exhibits poor selectivity due to competitive combustion. Moreover, conversions should be kept low to control overoxidation and heat generation.

On the other hand, sodium hypochlorite and hydrogen peroxide have emerged as useful reagents to perform oxidations under mild reaction conditions and without metallic waste.\textsuperscript{6,7} Bleach is particularly inexpensive as witnessed by its use to inhibit microbial growth in swimming pools, whereas H\textsubscript{2}O\textsubscript{2} has recently been used in the manufacture of bulk chemicals such as propylene oxide.\textsuperscript{8} Indeed, the progress of process technology and the increasing economies of scale allowed the manufacturing cost of H\textsubscript{2}O\textsubscript{2} to decrease. Moreover, new promising methods will probably make this reagent still cheaper.\textsuperscript{7,8}

2.1. Hydrogen Peroxide. Excluding oxygen, H\textsubscript{2}O\textsubscript{2} is the most valuable oxidant with an atom efficiency of 47%,\textsuperscript{9} generating water as the only byproduct. Lipophilic quaternary ammonium salts such as Alquat 336 or HexaN'Br\textsuperscript{−} are capable to efficiently extract H\textsubscript{2}O\textsubscript{2} from the aqueous to the organic phase, allowing fast oxidation reactions under PTC conditions.\textsuperscript{9}

In some cases the H\textsubscript{2}O\textsubscript{2} oxidation processes are accelerated by the addition of molybdates or wolframates as cocatalysts.\textsuperscript{10}

For example, a halide and organic solvent free oxidation of 2-hexanone and secondary alcohols with H\textsubscript{2}O\textsubscript{2} under liquid–liquid (LL) PTC conditions afforded the corresponding carboxylic acids and ketones with high yields in short reaction times.\textsuperscript{11}

The direct oxidation of cyclohexene 1 to adipic acid 2 is one of the most remarkable oxidation reactions under PTC conditions (Scheme 1).\textsuperscript{10}

In fact, adipic acid is manufactured as much as 3.5 million tons, mainly for nylon-6.6 production. However, the classical commercial process relies on a hazardous cyclohexane air oxidation providing a mixture of cyclohexanol and cyclo-

Scheme 1. Cyclohexene Route to Adipic Acid

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hexaneone, followed by nitric acid oxidation that generates large amounts of the greenhouse gas N₂O as byproduct. The cyclohexene route, originated from the development of selective hydrogenation of benzene to cyclohexene, enables a more efficient approach requiring less hydrogen and generating lower amounts of byproducts.

The cyclohexene oxidation proceeds through extraction in the organic phase of a bisperoxotungstic acid species, initially formed in the aqueous phase by Na₂WO₄·2H₂O and 30% H₂O₂ by the quaternary ammonium salt. After releasing oxygen, the reduced monoperoxo tungstate ion is reoxidized by H₂O₂ to initiate a new cycle.

Although the cyclohexene pathway can solve environmental and safety problems related to the current commercial process, it still does not appear to be competitive due to the low selling price of adipic acid. Several other approaches have been investigated by using organic ligands or acidic promoters, instead of Pt catalysts, even in flow processes.

Unsaturated fatty acids have been oxidized under acidic PTC conditions by reaction with 30% H₂O₂ in the absence of organic solvents, affording moderate to good yields of the related dicarboxylic acids 3 (Scheme 2). This protocol allows the synthesis of carboxylic acids from renewable feedstocks and constitutes a more sustainable approach to this class of compounds currently generated by oleic acid ozonolysis that suffers from high energy demand, toxicity of ozone, and safety risks.

Hydrogen peroxide has also been used for the one-pot conversion of cyclohexanol to ε-caprolactam in the presence of ammonium tungstophosphoric salt (n-C₁₆H₃₃NMe₃)-H₂PW₁₂O₄₀. Although an ammonium sulfate free technology has been developed, based on ENI TS-1 ammoximation followed by catalytic rearrangement, ε-caprolactam is manufactured mainly by the cyclohexanone oxime process generating huge amounts of ammonium sulfate and suffering from corrosion caused by fuming sulfuric acid. Therefore, this approach may result in a simple and practical approach to the synthesis of ε-caprolactam.

### 2.2. Sodium Hypochlorite

Oxidations of alcohols to aldehydes/ketones or carboxylic acids with aqueous NaClO under PTC conditions have been previously reported. More recently the same reactions have been investigated under continuous flow conditions at room temperature (rt) by mixing an organic solution of the substrate and Bu₄N⁺Br⁻ (TBAB) with 12.6% sodium hypochlorite. Biphasic reactions in flow benefit from high surface area to volume ratio providing better mass and heat transfer. Secondary aliphatic and benzylic alcohols 4 can be oxidized to ketones 5, whereas benzylic alcohols 6 can be selectively oxidized to esters 7 or aldehydes 8, depending on the reaction conditions (Scheme 3). In fact, when the same reactions have been carried out in the presence of excess MeOH, the methyl esters were obtained, likely through the oxidation of a hemiacetal formed in situ. Complete conversions can be obtained in short reaction times (5–30 min).

### Scheme 2. Oxidation of Unsaturated Fatty Acids

| Oleic, Linoleic, Erucic Acid | H₂O₂, 90 °C, 24 h | H₂PO₄ (5 mol%) | PTC (10 mol%) | Na₂WO₄·2H₂O (5 mol%) | 54–82% conversions can be obtained in short reaction times (5 min).

### Scheme 3. Oxidation of Alcohols in Flow under PTC Conditions

The production rate of these reactions has been increased up to 700 times by the proper choice of the microreactor.

### 2.3. Oxygen

The solvent free autoxidation of methylbenzenes 9 to benzoic acids 10 has been obtained with high conversion in the presence of CoCl₂·6H₂O, N-hydroxyphthalimide (NHPi), and didecyl dimethylammonium bromide (DDAB) by sparging oxygen through the solution at 80 °C (Scheme 4). This ternary catalytic system outperformed previous results in NHPi promoted autoxidation of hydrocarbons since the PT catalyst allows the solubilization of NHPi (otherwise poorly soluble in apolar media), at the same time preventing its degradation. Indeed, after complete conversion, the reaction started again at the same rate when a second batch of the starting material was added.

Photooxygenation of β-keto esters 11 through air oxidation in the presence of tetraphenyl porphine (TPP) as a sensitizer afforded hydroxylated compounds 12 in high yields and good ee’s under LL-PTC conditions, with a cinchonine based ammonium salt 13 (Scheme 5). The authors provided evidence for the involvement of ¹⁰O₂ in the hydroxylation reaction.
The same authors had previously described the hydroxylation of \( \beta \)-keto esters with a cinchonine based ammonium salt and commercially available cumyl hydroperoxide as oxidant.\(^{25}\)

### 2.4. Potassium Permanganate

Potassium permanganate oxidation of alkenes has been an established reaction since the dawn of PTC. A new pillar[5]arene macrocyclic PT catalyst \(^{15}\) has recently shown high substrate selectivity in the oxidative cleavage of linear short alkenes in the presence of branched alkenes (Scheme 6).\(^{26}\) The authors ascribed the selectivity observed in the competitive oxidation of 1-hexene to 1-pentanal and 4-methyl-1-hexene to 3-methyl-1-pentanal (85/7) to the host–guest complexation between the catalyst and the olefin.\(^{26}\) A new approach to asymmetric dihydroxylation has been explored through the permanganate promoted oxidative cyclization of achiral 1,5-dienes \(^{16a}\) in the presence of a chiral PT catalyst \(^{17}\) that could generate tetrahydrofuran diols \(^{18}\) in a single step (Scheme 7).\(^{27}\)

In the case of trisubstituted enoates \(^{23}\) (\(Z,E\) mixture), it was found that the best results could be obtained under acidic conditions affording 2-hydroxy-3-oxo derivatives \(^{24}\) in good to excellent yields and ee’s (Scheme 9). The stereoselectivity obtained points out that both \(Z\)- and \(E\)- substrates were transformed to the same enantiomer.

### 2.5. Potassium Peroxomonosulfate

Potassium peroxyoxonosulfate \(\text{KHSO}_3\)\(^{30}\) is an inorganic, stable, water-soluble, and environmentally safe oxidant. It is also commercially available and inexpensive; therefore, it has been used under PTC biphasic conditions for various oxidations such as the alkene epoxidation through in situ dimethyl dioxirane generation.\(^{31}\) More recently various phenols \(^{25}\) have been converted regioselectively to \(o\)-quinones \(^{26}\) under solid–liquid (SL) PTC conditions in the presence of catalytic amount of 2-iodobenzenesulfonic acid (proIBS) and oxone as co-oxidant (Scheme 10).\(^{32}\)

Although several examples of phenol to quinones oxidation have been previously reported, they all used stoichiometric conditions finding the best results could be obtained under acidic conditions affording 2-hydroxy-3-oxo derivatives in good to excellent yields and ee’s (Scheme 9). The stereoselectivity obtained points out that both \(Z\)- and \(E\)- substrates were transformed to the same enantiomer.

### Scheme 6. Substrate Selective Oxidation of Alkenes

```
\[14a\] \text{EtOCC=CH}_2 \xrightarrow{\text{KMnO}_4, 15 (0.9 mol\%)} \text{EtOC(O)CH}_2\text{H} \\
\[14b\] \text{EtOCC=CHCH}_3 \xrightarrow{\text{KMnO}_4, 15 (0.9 mol\%)} \text{EtOC(O)CH}_2\text{H}
```

In the case of trisubstituted enoates \(^{23}\) (\(Z,E\) mixture), it was found that the best results could be obtained under acidic conditions affording 2-hydroxy-3-oxo derivatives \(^{24}\) in good to excellent yields and ee’s (Scheme 9). The stereoselectivity obtained points out that both \(Z\)- and \(E\)- substrates were transformed to the same enantiomer.

### Scheme 7. Permanganate Promoted Asymmetric Dihydroxylation

```
\[16a\] \text{ArCOCH}_2\text{Br} \xrightarrow{\text{KMnO}_4 (1.6 eq), AcOH (6.5 eq), 20 \text{h}, -30 ^\circ \text{C}} \text{ArCO(O)CH}_2\text{Br} \\
\[16b\] \text{PhCOCH}_2\text{Br} \xrightarrow{\text{KMnO}_4 (1.5 eq), 17 (1 eq), 20 \text{h}, -60 ^\circ \text{C}} \text{PhCO(O)CH}_2\text{Br}
```

In the case of trisubstituted enoates \(^{23}\) (\(Z,E\) mixture), it was found that the best results could be obtained under acidic conditions affording 2-hydroxy-3-oxo derivatives \(^{24}\) in good to excellent yields and ee’s (Scheme 9). The stereoselectivity obtained points out that both \(Z\)- and \(E\)- substrates were transformed to the same enantiomer.

### Scheme 8. Dihydroxylation of \(\alpha\)-Arylacrylates

```
\[19a\] \text{ArCO}_2\text{Bu'} \xrightarrow{\text{KMnO}_4 (1.5 \text{ mol eq})} \text{ArCO}_2\text{Bu'}
```

In the case of trisubstituted enoates \(^{23}\) (\(Z,E\) mixture), it was found that the best results could be obtained under acidic conditions affording 2-hydroxy-3-oxo derivatives \(^{24}\) in good to excellent yields and ee’s (Scheme 9). The stereoselectivity obtained points out that both \(Z\)- and \(E\)- substrates were transformed to the same enantiomer.

### Scheme 9. PTC Route to 2-Hydroxy-3-oxoesters

```
\[19b\] \text{ArCO}_2\text{Bu'} \xrightarrow{\text{AcOH}, \text{K MnO}_4 (1.5 \text{ eq})} \text{ArCO}_2\text{Bu'}
```

In the case of trisubstituted enoates \(^{23}\) (\(Z,E\) mixture), it was found that the best results could be obtained under acidic conditions affording 2-hydroxy-3-oxo derivatives \(^{24}\) in good to excellent yields and ee’s (Scheme 9). The stereoselectivity obtained points out that both \(Z\)- and \(E\)- substrates were transformed to the same enantiomer.

### Scheme 10. PTC Route to 2-Hydroxy-3-oxoesters

```
\[20\] \text{ArCO}_2\text{Bu'} \xrightarrow{\text{AcOH}, \text{K MnO}_4 (1.5 \text{ eq})} \text{ArCO}_2\text{Bu'}
```

In the case of trisubstituted enoates \(^{23}\) (\(Z,E\) mixture), it was found that the best results could be obtained under acidic conditions affording 2-hydroxy-3-oxo derivatives \(^{24}\) in good to excellent yields and ee’s (Scheme 9). The stereoselectivity obtained points out that both \(Z\)- and \(E\)- substrates were transformed to the same enantiomer.

Although several examples of phenol to quinones oxidation have been previously reported, they all used stoichiometric conditions finding the best results could be obtained under acidic conditions affording 2-hydroxy-3-oxo derivatives in good to excellent yields and ee’s (Scheme 9). The stereoselectivity obtained points out that both \(Z\)- and \(E\)- substrates were transformed to the same enantiomer.
amounts of hypervalent iodine(V) compounds and dipolar aprotic solvents such as DMF. Therefore, this PTC procedure represents a more practical and efficient method to generate these useful intermediates for the synthesis of biologically important compounds. The regioselectivity observed has been tentatively ascribed to the formation of a iodine(V)−phenol complex from 2-iodoxy benzenesulfonic acid (IBS), formed in situ by oxidation of proIBS with Bu4N+HSO5−. After oxygen transfer and o-quinone formation, the catalytic cycle can proceed by successive oxidations by Bu4N+HSO5−. It is worth noting that the same reaction afforded mainly p-quinones when carried out in aqueous acetonitrile.

The oxidation of benzylic methylene compounds to ketones was realized with good-to-excellent yields through a similar approach. Various alkanes were also found to be reactive, although lower yields of oxygenated products could be obtained.

One of the most remarkable features of PTC is the possibility to perform reactions in an aqueous/organic biphasic mixture without hydrolysis of sensitive organic reagents or products. In fact, water phase serves as reservoir of inorganic reagents to be extracted in the organic phase by the PT catalyst. However, the interphase protects the hydrolysis-sensitive organic compounds from hydrolysis. An example of this is the preparation of ε-caprolactone hydrolysis was formed as a single product.

### 2.6. Epoxidation

A chiral secondary amine catalyst has been used in the epoxidation of simple olefins by using oxone as the stoichiometric oxidant under PTC conditions. Enantiomerically enriched α,β-epoxyketones are versatile building blocks that have been obtained previously from enones with a variety of efficient strategies under PTC conditions using practical oxygen sources such as NaClO or H2O2.

A new type of bis-quaternary cinchonidine based ammonium bromides has been used for the oxidation of a variety of chalcones to the corresponding epoxides with excellent yield and enantioselectivity.

### 2.7. Disubstituted enones proved to be quite recalcitrant substrates toward epoxidation. In particular, β,β-disubstituted enones 37 bearing a trifluoromethyl group could not be converted to the corresponding epoxides 39 until the asymmetric aerobic oxidation, induced by H2N-NHMe and catalyzed by the cinchonidinium salt 38, was recently discovered. The authors proposed that this epoxidation proceeds through the in situ generation of highly reactive and pure H2O2. In fact, when 50% H2O2 was used instead of the air/base/methylhydrazine system, the same stereoselectivity was observed, although in a lower 66% yield.

A more practical approach has been developed by using 30% H2O2 as oxidant in the presence of a pentafluorobenzyl...
Scheme 15. Aerobic Epoxidation of β-Trifluoromethyl-β,β-disubstituted Enones

Scheme 16. Asymmetric Enone Epoxidation

Scheme 17. Synthesis of β-Halogenated Ketones

to give the spiroketeone 43a (Scheme 17). The authors propose
mechanism hypothesis based on the investigation on
substituent effect and kinetic isotopic effect of the fluorina-
tion/semipinacol reaction.

ACDC promoted by TRIP and its derivatives 44 was applied
to several transformations mediated by oxidative halogenation,
such as the fluorination/cyclization of N-allyl amides to
oxazolines, fluorination of enamides and, more recently,
to the halocyclization of benzanilides such as 45a,11
fluorocyclization of homologue benzamides 45b with Select-
fluor and Cy-TRIP (44a),17 and to the α-fluorination of
cyclohexanones,17 e.g., 46 (Scheme 18).

An analogous strategy was applied to the conversion of allylic
alcohols 47 into the corresponding α-fluoro homoallylic
alcohols.48 The fluorination–elimination process is 316
promoted by the in situ transformation of the alcohol into an
arylboronic ester 48. This function, in conjunction with a
TRIP-derived PT anionic agent, operates as temporary
enantiodirecting group.

This anionic PTC concept has been also exploited for the
asymmetric fluorolactonization of vinylbenzoic acids 50 to
give fluorinated isobenzofuranones 52 in high ee’s (Scheme 19) in
the presence of a new chiral binaphthyl catalyst 51.49

Classical cationic PTC conditions have been applied to the
electrophilic α-chlorination of activated methylene compounds
53 (Scheme 20),50 such as 1,3-diketones (X = Ar), β-keto
esters or amides (X = OR or NHPh), and nitriles 54. This
metal-free protocol employs NaCl as chloride source and the
hypervalent iodine compound IBX-SO3K as mild oxidant for
the umpolung of halide reactivity. A lipophilic quaternary
ammonium chloride as PT catalyst is necessary for good
conversion of the starting material.

The asymmetric chlorination of β-keto ester 55a has been
carried out by using N-chloro succinimide (NCS) as
chlorinating agent in the presence of a binapthyl derived
chiral phosphonium salt 56 (Scheme 20).51 A similar activated
ester 55b was α-fluorinated with high ee’s by using N-
fluorobenzenesulfonylimide (NFSI) in the presence of a PT
catalyst 57 containing a urea or thiourea unit.52 This family of
symmetric catalysts were also found to be effective in the
Michael addition of glycine Schiff bases to various Michael
acceptors and in the aldol-initiated cascade reaction.

Finally, manganese tetraphenyl- and tetramesityl porphyrin
promote the NaOCl chlorination of unactivated aliphatic
hydrocarbons in the presence of TBAB under LL-PTC
conditions.54

3. HALOGENATION

The importance of halogenated organic molecules both as
intermediates for further transformations and biologically active
compounds stimulated the study for alternative new syntheses
of these compounds. PTC oxidative introduction of halogens is
carried out by addition to an olefinic bond of a halogen cation
or by methylene functionalization of activated compounds by
this species and by halogen radical H substitution on a
unactivated sp³ carbon atom.

A recent report reveals the application of the asymmetric
counteranion-directed catalysis (ACDC) to the enantiose-
lective synthesis of β-halogenated by semipinacol rearrange-
ment of α,α-disubstituted allylic alcohols 41 (Scheme 17).11

The intermediate haliranium cation 42 (X = F, Cl, Br, I)
arraignes through a Wagner–Meerwein alkyl migration to the
haloketones 43. The haliranium formation is promoted by a
chiral PT catalyst formed in situ from the anion of liposoluble
eanitopure stericly crowded BINOL-phosphoric acid, with
an achiral cationic insoluble halogenating agent, e.g., Select-
fluor, in the fluorination reactions. This strategy allows to
inhibit the undesired background reaction leading to racemic
products due to poor contact between the reactant and the
halogenating agent located in different phases.

For example, the strained allylic alcohol 41a reacts with the
sodium salt of nonracemic phosphoric acid 44a and Selectfluor

References

1. Review

2. s16

3. quinidine-derived ammonium salt 40 (Scheme 16). Also this
simplified protocol, that does not use an hazardous compound
such as methylhydrazine, afforded β-trifluoromethyl-α,β-epoxy
ketones 39 with high yield and enantioselectivity.

4. Chiral octahedral complexes of Co(III) have also recently
been used as catalysts for the asymmetric epoxidation of
chalcones under PTC conditions, although with moderate
ee’s.10

5. 3. HALOGENATION

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Finally, manganese tetraphenyl- and tetramesityl porphyrin
promote the NaOCl chlorination of unactivated aliphatic
hydrocarbons in the presence of TBAB under LL-PTC
conditions.54

References
4. C–H ALKYLATION

In the last 25 years asymmetric PTC has become a reliable methodology to generate a variety of compounds under mild conditions. The first successful alkylation of N-(diphenylmethylene)glycine tert-butyl ester has become a standard benchmark reaction to test the new PT catalysts that have been introduced during these years. Many excellent reviews have appeared on the topic covering the literature until the middle of 2012, therefore, only the latest applications are reported herein.

The alkylation of \( \alpha \)-acetamidomalonates 58 under PTC conditions with the chiral binaphthyl catalyst 59 afforded the \( \alpha \)-acetamido-\( \alpha \)-alkylmalonates 60 in high yields and ee’s (Scheme 21). The two different ester groups, responsible for the stereoselectivity observed in the enolate alkylation, can be selectively hydrolyzed under acidic or catalytic hydrogenation and alkali basic conditions, thus facilitating further transformations toward the synthesis of various chiral compounds bearing a quaternary carbon center. More versatile \( \alpha, \alpha \)-dialkylmalonates 63 have been obtained through double PTC alkylation of 4-bromo benzylideneamino tert-butyl \( \alpha \)-methylmalonate (61) since the intermediate 4-bromobenzylxilometry ester 62 could be selectively hydrolyzed by 1N NaOH (Scheme 21).

A new class of easily accessible positively charged Co(III) chiral complexes 65 have been used in the benchmark alkylation of N-(diphenylmethylene)glycine tert-butyl ester with ee’s up to 94% (Scheme 22). The nucleophilic opening of racemic 2,2-disubstituted aziridines 66 by 3-alkyl oxindoles, under SL-PTC conditions, afforded the 3-alkylated compounds 68 bearing two contiguous all carbon quaternary stereocenters with excellent yields and ee’s (Scheme 23). This ring opening, which is catalyzed by the chiral 1,2,3-triazolium salt 69, represents an unusual case of completely regioselective attack at the more substituted carbon of the aziridine ring.

The ring opening of aziridines have also been exploited to generate quaternary carbon stereogenic atoms bearing ethylene-amino and propylene-amino moieties in a highly enantioselective and diastereoselective fashion by using a chinchona alkaloid-derived PT catalyst bearing the bulky adamantoyl ester group. A variety of indolenines 72 have been generated in good to excellent ee’s from 2-(2-isocyanoaryl)-2-arylacetonitriles 70 by an intramolecular 5-endo-dig cyclization of the benzylic carbanion onto the o-nitroil group carried out in the presence of the chinchona catalyst 71 (Scheme 24). Indolenines has been reduced in situ to stable indolines or reacted under acidic conditions with electron rich aromatics such as 3-(dimethylamino)phenol to give 2-substituted indoles without erosion of ee. The stereoselectivity observed was strongly influenced by the PT catalyst used. The best
399 results have been obtained with a tailored bifunctional catalyst bearing a Brønsted acid site capable to activate the isonitrile, thus favoring a preorganized transition state along with the chiral cation.

The enantioselective nucleophilic aromatic arylation ($S_N Ar$) of β-keto ester $55c$ with activated aromatic fluorides has been realized under PTC conditions with the benzoylated cinchonidinium salt $75$ (Scheme 25).

Moreover, the $S_N Ar$ of 3-aryloxindoles $76$ on aryl fluorides with the binaphthyl bifunctional quaternary phosphonium bromide $77$ (Scheme 26) as PT catalyst, afforded triaryl methanes $78$ with good to high enantioselectivities.

However, both methods suffer from limited scope, since only electron-deficient fluoroarenes could be employed. On the contrary, less reactive fluoroarenes could be activated by forming the corresponding arene-chromium complexes. The $\alpha\text{-}\alpha$ arylation of various $\alpha\text{-}\alpha$-amino acid derivatives $79$ with chromium complexes $80$ derived from electron donating fluoroarenes under LL−PTC conditions with binaphthyl modified chiral PT catalyst $81$ afforded $\alpha\text{-}\alpha$-disubstituted $\alpha\text{-}\alpha$-amino esters $82$ with good yield and high ee's after treatment with aqueous HCl for...
420 hydrolysis of the imine moiety and removal of chromium
421 (Scheme 27).65
A highly enantioselective alkylation of ν-H-oxazol-4-ones
422 with benzyl and allyl bromides has been carried out under SL-
423 PTC conditions, by using a L-tert-leucine derived urea-
424 ammonium salt (Scheme 28).66 Although a huge excess of
425 alkylating agents was required, a variety of dialkylated
426 compounds could be generated with good yields and high
427 ee’s, thus giving access to useful chiral ν-hydroxy carboxylic
428 acids or amides by simple functional group manipulations.

5. BASE-FREE PTC

Some quite reactive substrates have been recently subjected to
431 asymmetric PT reactions in the absence of base.7 A lipophilic
432 bifunctional ammonium or phosphonium salts have shown to
433 be essential for the outcome of the reactions. It is also worth
434 noting that the aqueous–organic system is crucial to obtain
435 high conversion. Indeed, the base-free reaction was sluggish
436 when carried out in a homogeneous system by using various
437 organic solvents under otherwise identical conditions. Amina-
438 tion of nitroolefins,8 conjugate additions of ν-substituted
439 nitroacetates to maleimide, and 3-substituted oxindoles9 to
440 acrolein, direct aldol reaction of ν-substituted nitroacetates
441 with aqueous formaldehyde, have all been performed
442 without base and in the presence of a binaphthyl-bifunctional
443 PT catalyst according the corresponding products in
444 s29 good to high yields and ee’s (Scheme 29).

6. DEPOLLUTION

The PTC capability to extract anions from the aqueous to the
445 organic phase has been used to destroy harmful nucleophiles
446 for example phenoxide and cyanide anions) present in low
447 concentrations in aqueous waste streams.8 The treatment of
448 the aqueous stream with a PT catalyst and an electrophilic
449 reagent (for example an alkyl halide) entails the 2-fold
450 advantage of purifying the waste stream generating at the
451 same time a saleable product, therefore increasing the
452 profitability of the whole process (Scheme 30). The
453 concentration of these anions in water decreased from 10 000
454 ppm to less than 1 ppm in 2–3 h at less than 70 °C.
455
A novel technology for depollution from toxic polyhalo-
456 genated compounds has been developed by using a mixture of
457 H2O2, NaOH in the presence of Aliquat 336 as PT catalyst
458 (Scheme 31).69 The reaction has been carried out at 298 K in
459 an adiabatic reactor in order to take advantage of the heat
460 released by the exothermic reaction to reach completion after
461
5–10 min only (T\textsubscript{max} of 343 K was reached after 1 min). Total destruction of various harmful polyhalomethanes and polyhalo-ethylenes has been obtained in 10 min according solid Na\textsubscript{2}CO\textsubscript{3} and NaCl.\textsuperscript{70} Formation of chlorine has also been proved by detection of (1,2-dichloroethyl)benzene by passing the effluent gas through a styrene trap.

The results led the authors to propose a reaction mechanism involving extraction of the nucleophilic superoxide anion by the PT catalyst into the organic phase (CCl\textsubscript{4} or other halogenated compound) where it rapidly converts CCl\textsubscript{4} to Na\textsubscript{2}CO\textsubscript{3} and NaCl. The technology seems to be promising for treating nonaqueous phase liquids (NAPLs) that are byproducts of many industrial processes and actually require extraction from water bulk.

7. SUMMARY AND OUTLOOK

This mini-review aims to illustrate the benefits of PTC in oxidation reactions through the most recent synthetic applications. The use of cheap and harmless oxidants such as NaClO and H\textsubscript{2}O\textsubscript{2} under PTC conditions allows to develop practical procedures. Moreover, toxic heavy metal species and dipolar aprotic solvents can be avoided thus cooperating to the sustainability of the PTC method.

Many industrial manufacturing processes take advantage of this methodology in order to develop more profitable alternatives to existing procedures by reducing the amount of waste and using milder reaction conditions. Continuous processes under PTC conditions has recently been investigated through microreactors or traditional equipment.\textsuperscript{72–71} Chiral anionic PTC has greatly expanded the scope of asymmetric halogenation whereas it has also been discovered that some reactive substrates may react under aqueous–organic biphasic systems without the need of any added base.

Bifunctional chiral ammonium salts have emerged as powerful catalysts to promote reactions in a highly stereoselective fashion.

New concept catalysts such as cycloprenium,\textsuperscript{72} pentanimium,\textsuperscript{73} and 2-oxopyrimidinium\textsuperscript{74} PT catalysts have also been recently developed and found to be effective even in enantioselective reactions.

In summary, the results presented here witness that after decades from its blossom PTC still arouses and promises a great deal of interest both in academia and industry due to its special features facilitating the development of new reaction paths and sustainable procedures.

**REFERENCES**


