Tetrahedron Letters Vol. 21, pp 2115 - 2118
0040-4039/80/0522-2115$02.00/0

TERTIARY AMINE OXIDES AS PHASE TRANSFER CATALYSTS FOR SUBSTITUTION AND DICHLOROCYCLOPROPANATION REACTIONS

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Summary: Tertiary amine oxides catalyze a variety of phase transfer reactions, primarily by in situ deoxygenation to form the tertiary amine or derived catalyst.

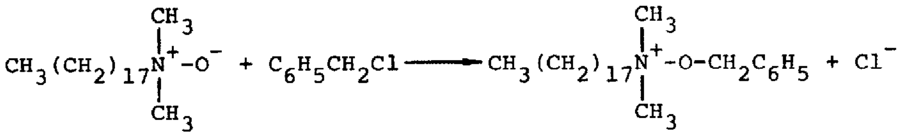
The two principal classes of compounds known to serve as phase transfer catalysts are the macrocyclic polyethers (crowns, cryptands, etc.) and quaternary 'onium salts (ammonium, phosphonium, arsonium, etc.).[1] Numerous other substances have shown catalytic activity, including the open-chained forms of many crowns (glymes,[2] polypodes[3]) and a host of tertiary amines.[4] In most cases, the latter compounds function as catalysts only after formation of the corresponding quaternary ammonium salts in situ.[4] Even polyamines such as tetramethylethylenediamine (TMEDA) are now known to function as simple tertiary amines and do so by formation of a quaternary ammonium salt in the reaction mixture.[5]

A class of compounds which seemed an obvious choice as a phase transfer catalyst is the tertiary amine oxides. These compounds ($R_3N^+-O^-$) contain a quaternary nitrogen atom but do not seem such a plausible prospect in the sense that their application to phase transfer processes would be limited by their inability to exchange covalently bound oxygen for some other anion. The recent patent reporting use of N,N-dimethyldodecylamine oxide as a phase transfer catalyst in a dichlorocarbene addition reaction[6] prompts us to report some of our own results using these materials as phase transfer catalysts.

N,N-Dimethyloctadecylamine oxide (Schercamox DMS®) catalyzes the two-phase reaction of potassium acetate with benzyl chloride in acetonitrile solution (eq. 1). In the absence of this catalyst, no reaction can be detected, even after 86,400 sec. In the presence of Schercamox DMS® (10 mol-%, 30°C) the reaction proceeds with a rate of 2.5 x 10^{-6} sec^{-1}.[7] The actual catalyst is apparently formed in situ by a redox reaction.[8]

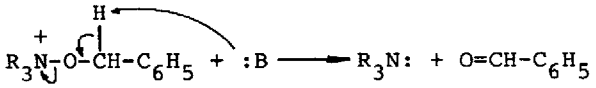
$$C_6H_5\text{-}CH_2\text{-}Cl + KOAc \xrightarrow[30^{\circ}C]{CH_3CN} C_6H_5\text{-}CH_2\text{-}OAc + KCl \qquad (1)$$

In the first step, the amine oxide reacts with benzyl chloride forming a quaternary ammonium ether (eq. 2). This charged species then undergoes deprotonation (perhaps by Cl^- or solvent) initiating a β-elimination (eq. 3). The products are a tertiary amine and benzaldehyde. The tertiary amine reacts further with benzyl chloride to form the catalytically active species: A quaternary ammonium salt (eq. 4).



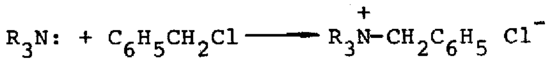
(2)

$$CH_3(CH_2)_{17}\overset{CH_3}{\underset{CH_3}{N^+}}-O^- + C_6H_5CH_2Cl \longrightarrow CH_3(CH_2)_{17}\overset{CH_3}{\underset{CH_3}{N^+}}-O-CH_2C_6H_5 + Cl^-$$



(3)

$$R_3\overset{+}{N}-O-\overset{H}{CH}-C_6H_5 + :B \longrightarrow R_3N: + O=CH-C_6H_5$$

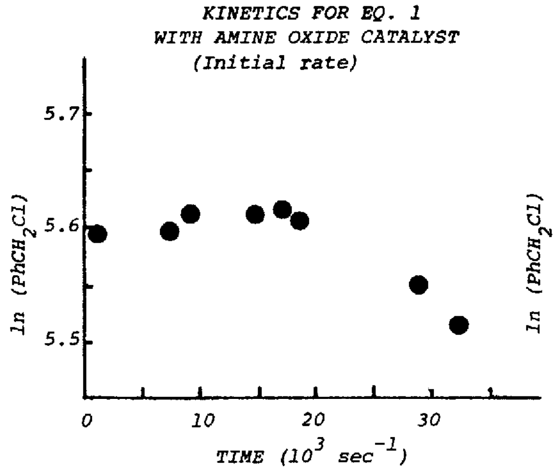


(4)

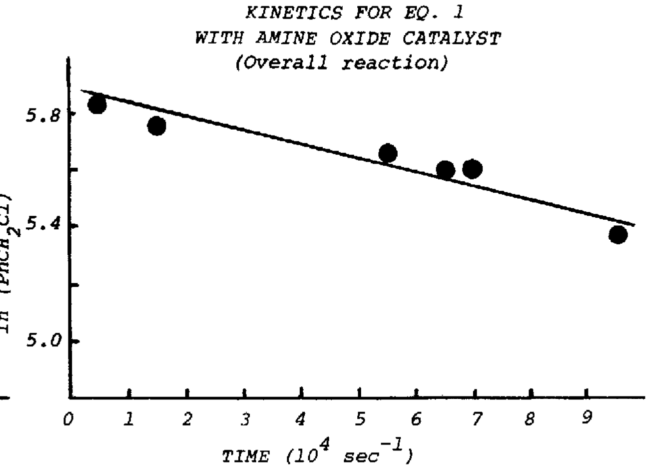
$$R_3N: + C_6H_5CH_2Cl \longrightarrow R_3\overset{+}{N}-CH_2C_6H_5\ Cl^-$$

There are three key features of the reaction mechanism which is presented here to account for the activity of the amine oxides. First, if the postulated mechanism is correct, benzaldehyde must be observed as a by-product, although only a small amount might be formed since the reaction should be catalytic. Second, there should be an observable induction period in the reaction during which the transformations described by equations 2-4 take place. Finally, the derived quaternary salt (eq. 4) must itself be capable of catalyzing the reaction in question.

For the system described by equation 1, glpc analysis (0.25 in x 5 ft, 10% SE-30 on NAW firebrick 60/80 mesh) indicated the presence of benzaldehyde, identified both by retention time and coinjection of a pure sample. An examination of the kinetic data shown on the graph below, indicates that there is clearly an induction period for this reaction. Finally, the ester formation reaction from benzyl chloride and potassium acetate has been investigated in considerable detail by several groups[4,5,9] and is, indeed, catalyzed by tertiary amines, via the derived quaternary ammonium salt. Indeed, even such low molecular weight amines as tetramethylethylene diamine catalyze this reaction[9] albeit by *in situ* quaternization of the amine.[5]



KINETICS FOR EQ. 1
WITH AMINE OXIDE CATALYST
(Initial rate)



KINETICS FOR EQ. 1
WITH AMINE OXIDE CATALYST
(Overall reaction)

The dichlorocyclopropanation reaction reported in the recent patent[6] presents a slightly more difficult problem. Although the carbene addition to simple olefins is known to be catalyzed by quaternary ammonium salts,[10] this reaction may also be catalyzed by tertiary amines.[11] The details of the latter mechanism have been worked out by Makosza and co-workers[12] and seems on firm footing. The question which must be answered is whether the amine oxide is actually the catalyst for the cyclopropanation, or if the catalyst is the tertiary amine derived from amine oxide. Some evidence for the latter possibility is found in our observation that in our hands, the dichlorocyclopropanation of styrene can be effected using either N,N-dimethyldodecylamine (72%) or the corresponding N-oxide (64%). Although the latter yield is lower than that claimed in the patent, we were unable to attain their yields even using benzyltriethylammonium chloride.[13]

The fact that the reaction can be catalyzed either by amine or amine oxide is not conclusive evidence for amine rather than amine oxide catalysis. The amine oxide could react with a small amount of dichlorocarbene generated at the interface as shown below, and this species could serve as the catalyst.

$$:CR_2 + R_3\overset{+}{N}\text{-}\overset{-}{O} \longrightarrow R_3\overset{+}{N}\text{-O-}\overset{-}{C}R_2 \qquad (5)$$

$$R_3\overset{+}{N}\text{-O-}\overset{-}{C}R_2 + HCCl_3 \longrightarrow R_3\overset{+}{N}\text{-O-}CR_2H\ Cl^- + :CCl_2 \qquad (6)$$

When we irradiated[14] diphenyldiazomethane (7.7 mmol)[15] and N,N-dimethyldodecylamine oxide (7.7 mmol) in the presence of a large excess of styrene and chloroform (154.6 mmol each), we found that both 1,1,2-triphenylcyclopropane[14] and 1,1-dichloro-2-phenylcyclopropane were produced (detected by glpc) but the former was favored over the latter by 28:1. While this experiment is not unequivocal, it is strongly suggestive of instability or ineffectual catalysis provided by a $R_3\overset{+}{N}\text{-O-}\ddot{C}Ph_2$ species.

The question of how the amine oxide is converted into the amine remains. There are at least three possible routes which appear feasible. In the first of these, the amine oxide attacks chloroform in the S_N2 sense in analogy to the reaction sequence described in eqs. 2-4. This seems unlikely to us since nucleophilic substitution at the sterically hindered chloroform carbon should not be a fast reaction. A second possibility is that the amine oxide is contaminated by a small amount of amine which generates enough dichlorocarbene to deoxygenate the amine oxide[16] and form additional catalyst. The process could be cyclic and the formation of a large amount of catalyst by this method is possible. This mechanism seems reasonable, however, only if the reaction rate between $:CCl_2$ and olefin is similar to but not significantly larger nor smaller than for deoxygenation. In the former case, only a trace of cyclopropanation product would be observed; in the latter, all of the carbene would be consumed before cyclopropanation could occur. The third, and most reasonable possibility is, in our opinion, that at 40-45°C as specified in the patent[6] the amine oxide simply decomposes[17] with formation of some tertiary amine and this is actually the catalytic species.

It seems likely to us from the above data and other information to be presented in the full report of this work, that in the case of tertiary amine oxides as in the case of other systems, a tertiary amine and/or the corresponding quaternary ammonium salt is the catalytically active species.

NOTES AND REFERENCES

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7. The rate constant is the average of two runs and is probably only of order of magnitude precision. Since the reaction has a substantial heterogenous component, we estimate that the error may be as high as 50%.

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(Received in USA 11 February 1980)