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# The Mechanistic Study and Synthetic Applications of the Base Treatment in the Ozonolytic Reactions

**Yung-Son Hon,*[a] Sheng-Wun Lin,[b] Ling Lu[a] and Yao-Jung Chen[b]**

[a] *Institute of Chemistry, Academia Sinica, Nankang, Taipei, Taiwan 11529, R.O.C.*

[b] *Department of Chemistry, National Chung-Hsing University, Taichung, Taiwan, R.O.C.*

**Abstract:** The E1cb mechanism is the overwhelming process in the reaction of bases and ozonides. As a quenching agent in the ozonolysis of a variety of alkenes, the reactions involving triethylamine often gave better yields and proceeded faster than those involving methyl sulfide. On the other hand, in the presence of 4 Å molecular sieves, the secondary amines reacted with mono- and 1,1-di-substituted ozonides to afford the reductive amination products in high yields. The formation of ammonium formate in the reaction mixture also supported the E1cb mechanism in the reaction of ozonide and amine.

## INTRODUCTION

Recently, we have reported that mono-substituted aliphatic ozonides reacted with stable phosphorus ylides to give the Wittig-type products in high yields.[1] The reaction mechanism probably involved the deprotonation of the ozonide ring by the phosphorus ylides; the ring fragmentation then occurred to give aldehydes as intermediates.[1c] In other words, the ozonide ring proton are removable by phosphorus ylides. This proposed reaction pathway is quite different from reductive workup conditions where the reducing agents, such as triphenylphosphine and methyl sulfide, attack ozonides at a peroxide oxygen atom to cause the fragmentation and give the corresponding carbonyl compounds.[2] Although triethylamine has been utilized to decompose the mono-substituted ozonides to give an aldehyde,[3] there is no clear conclusion about its mechanism. For example, Razumovskii *et al.* found that the first step of the reaction between amine and ozonide in polar media resulted in cation-radicals of the amines, while in nonpolar media there were found radicals of *N*-oxides. Apparently, the electron transfer process occurred from the reaction of amine and ozonides.[4] However, Ellam *et al* suggested that the reaction of stilbene ozonide with amine probably followed the acid-base process.[5] In this report, we described our approach to clarify the reaction mechanism between ozonide and amines and extend their synthetic applications.

## RESULTS AND DISCUSSION

### I. The Role of Amines in their Reaction with Ozonides

Since tertiary amine can be oxidized to the amine *N*-oxide by hydrogen peroxide, it is interesting to know the real reaction pathway between amines and ozonides. In order to differentiate the acid-base and oxidation-reduction process properly, the bicyclic ozonide (**2**) was designed for this purpose. The keto-aldehyde (**3**) was formed if the nucleophilic attack of amine on the peroxide linkage followed by fragmentation occurred. On the other hand, the keto-acid (**4**) was formed if the deprotonation of the bridgehead proton by amine followed by fragmentation occurred (Scheme 1). Therefore, we can easily differentiate the role of amine in its reaction with ozonides by the product distribution.

**Scheme 1**

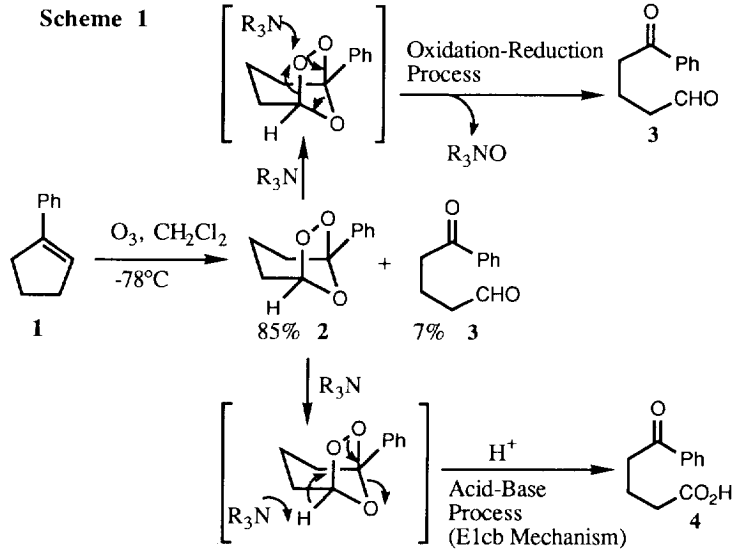



**Table 1** The reaction of bicyclic ozonide ( **2**) with various reagents at room temperature

| entry | reagents | time | yield (%) **3** | **4** |
|---|---|---|---|---|
| 1 | $Et_3N$ | 1h | – | 99 |
| 2 | i-$Pr_2NEt$ | 1h | – | 98 |
| 3 | Pyridine | 72h[a] | – | 97 |
| 4 | 2,6-Lutidine | 19h[a] | – | 97 |
| 5 | $Me_2S$ | 72h | 92 | 7 |
| 6 | $Ph_3P$ | 12h | 97 | – |

[a] It took several days for the reaction to complete. The reaction was sped up by heating up to reflux in $CH_2Cl_2$ .

According to literature procedure[6], 1-phenylcyclopentene **1** prepared from cyclopentanone by addition with phenylmagnesium chloride and subsequent dehydration with *p*-toluenesulfonic acid, was treated with ozone in dichloromethane at -78 °C to afford ozonide **2** in 85% and 5-oxo-5-phenylpentanal (**3**) in 7% yields. They were separated by silica gel column chromatography and bicyclic ozonide (**2**) was then treated with various reagents in $CH_2Cl_2$ at room temperature. The crude products were purified by column chromatography and the results were summarized in Table 1. Since the keto-acid (**4**) was formed as the sole product when triethylamine, Hünig base, pyridine, or 2,6-collidine was utilized to decompose the ozonide **2**, it is clear that the role of these nitrogen-containing reagents is to abstract the bridgehead proton only (entries 1-4). The reaction of ozonide **2** and pyridine is a slow process and it took 72 h to complete the reaction under refluxing condition in $CH_2Cl_2$ (entry 3). In this particular case, the reaction mixture was concentrated under reduced pressure to remove the excess pyridine and the crude mixture was directly injected to the gas chromatography. No pyridine *N*-oxide was detected by this technique.[7] Apparently, the pyridine was also not oxidized by the ozonide. On the other hand, the role of $Ph_3P$ is to attack the peroxide linkage to form the keto-aldehyde (**3**) as the sole product (entry 6). It is interesting to point out that both keto-aldehyde (**3**) (92%) and keto-acid (**4**) (7%) were formed when $Me_2S$ was used (entry 5). Although keto-acid (**4**) is a minor product, it demonstrated that the Lewis basicity of $Me_2S$ is enough to abstract the ozonide ring proton. In general, the reaction rates for tertiary amines and $Ph_3P$ are much faster than the other reagents (entries 1, 2 and 6).

In summary, the reaction of ozonide **2** with amine- or pyridine-like reagents followed the acid-base process, which is equivalent to the E1cb mechanism.[8] Redox is the only process when $Ph_3P$ was used. Interestingly, both of these two processes occurred when $Me_2S$ was used. This conclusion is consistent with Ellam's hypothesis,[5] but not with the results from EPR studies.[4] Tanner *et al.* pointed out that EPR-active materials can be detected at very low concentration ($>10^{-7}$ M) and the observation of an EPR spectra is not a conclusive indication that the major pathway involved the single electron transfer process.[9] In the fouth part of this discussion session, there is an additional evidence to support our conclusion.

### II. The best base in the decomposition of the mono-substituted ozonide

There are two different ozonide ring protons in the mono-substituted ozonides. It is interesting to know what is the best reagent to abstract the mono-substituted ozonide ring protons regioselectively. Only high regioselectivity can make this methodology useful in organic synthesis. Since the ozonides are made from terminal olefins in excellent yields[10], its isolation can be omitted. The ozonide (**6a**), prepared from the ozonolysis of the 1-decene in $CH_2Cl_2$ at -78 °C, was treated with inorganic bases in the same flask. Both the 1-nonanoic acid **9a** and the α,β-unsaturated aldehyde (**8a**) were formed when KO*t*-Bu, LiOH or NaH was used (Scheme 2 and entries 1-4, Table 2). The *E*– configuration of **8a** was determined unambiguously by 2D-NOSEY technique. Presumably, α,β-unsaturated aldehyde (**8a**) was formed from the base-catalyzed aldol condensation of the 1-nonanal (**7a**) (entries 1-4). Thus, inorganic bases such as KO-Bu-t, LiOH, and NaH are not suitable to decompose the mono-substituted ozonides due to the poor regioselectivity and the further condensation. However, the aldol condensation could be avoided if the ozonide **6a** was treated with methanolic $K_2CO_3$ in 1 h (entry 5).

When triethylamine or Hünig base was used, we found that ozonide **6a** was decomposed to give 1-nonanal **7a** as the major product in high yield within 1 h (Table 2, entries 7 and 8). No aldol condensation product was

**Scheme 2**

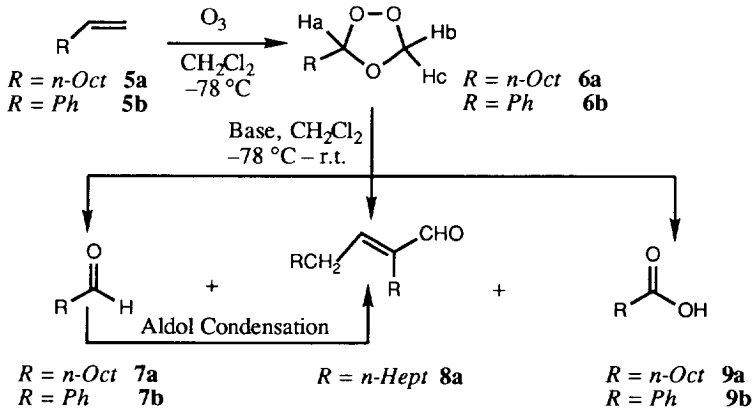



**Table 2** Reaction of 1-decene ozonide **6a** with bases

| entry | bases | time (h) | yield(%)[d] 7a | 8a | 9a |
|---|---|---|---|---|---|
| 1 | 2.2 eq. KOBu-t [a] | 1 | 0 | 39 | 47 |
| 2 | 1.1 eq. KOBu-t [a] | 1 | 0 | 37 | 39 |
| 3 | 1.1 eq. LiOH [b] | 16 | 0 | 26 | 62 |
| 4 | 1.1 eq. NaH [a] | 5 | 0 | 37 | 52 |
| 5 | 1.1 eq. $K_2CO_3$ [c] | 1 | 80 | 0 | 20 |
| 6 | 1.1 eq. $K_2CO_3$ [c] | 16 | 72 | 10 | 18 |
| 7 | 2 eq. $Et_3N$ | 1 | 82 | 0 | 18 |
| 8 | 2 eq. i-$Pr_2NEt$ | 0.6 | 79 | 0 | 11 |
| 9 | 2 eq. Pyridine | 72 | 50 | 0 | 33 |
| 10 | 2 eq. 2,6-Lutidine | 23 | 51 | 0 | 47 |
| 11 | 10 eq. $Me_2SO$ | 240 | 59 | 0 | 11 |
| 12 | 10 eq. DMF | 120 | 45 | 0 | 45 |
| 13 | 10 eq. $Me_2S$ | 72 | 71 | 0 | 14 |
| 14 | 2 eq. $Ph_3P$ | 12 | 82 | 0 | 0 |

THF[a], 50% THF/$H_2O$[b], and MeOH[c] were used as co-solvent, respectively. [d] The isolated yields were reported.

**Table 3** Reaction of styrene ozonide **6b** with base or reducing agent

| entry | bases | time (h) | yield(%)[a] 7b | 9b |
|---|---|---|---|---|
| 1 | 2 eq. $Et_3N$ | 1 | 18 | 78 |
| 2 | 2 eq. i-$Pr_2NEt$ | 1 | 29 | 62 |
| 3 | 2 eq. Pyridine | 18 | 14 | 81 |
| 4 | 2 eq. 2,6-Lutidine | 1 | 8 | 90 |
| 5 | 10 eq. $Me_2SO$ | 18 | 18 | 79 |
| 6 | 10 eq. DMF | 72 | 16 | 81 |
| 7 | 10 eq. $Me_2S$ | 24 | 38 | 60 |
| 8 | 2 eq. $Ph_3P$ | 10 | 96 | 0 |

[a] The chemical yield and product ratio of these reactions were determined by GC with hexadecane as the internal standard.

observed in each cases. When the bases in the pyridine families or the neutral reagents such as DMSO and DMF were used, the reaction rate is rather slow and significant amount of the 1-nonanoic acid **9a** was formed (entries 9-12). It is interesting to point out that both 1-nonanal **7a** (71%) and 1-nonanoic acid **9a** (14%) were formed when the Me2S was used (entry 13). However, only 1-nonanal **7a** was formed when the Ph3P was used (entry 14).

In general, the reaction rate of the base treatment is much faster than those of the reducing agents treatment. As far as the reaction rate and chemical yield were concerned, methanolic $K_2CO_3$, Hünig base and triethylamine are useful reagents to convert the mono-substituted aliphatic ozonide to the corresponding aldehyde. Their chemical yields are comparable to that of $Ph_3P$ treatment and are better than that of $Me_2S$ treatment.

We are interested in understanding the effect of the nature of the ozonide substituent on the regioselectivity in the reaction of base with ozonide. Therefore, the ozonide (**6b**) from styrene was prepared at -78 °C in pentane in 75% yield.[11] The purified ozonide (**6b**) was treated with a variety of organic bases in $CH_2Cl_2$ at room temperature (Scheme 2, Table 3). The benzoic acid (**9b**) instead of benzaldehyde (**7b**) was formed as the major product in all cases except when $Ph_3P$ was used. In comparison with $H_b$ (or $H_c$), the steric hindrance surrounding $H_a$ is larger. However, the deprotonation of $H_a$ become easier than that of $H_b$ (or $H_c$) due to the electron-withdrawing property of the phenyl group.[1c] The 2,6-lutidine provided the best yield in the formation of the benzoic acid (entry 4). Similar results were obtained when triethylamine, pyridine, DMSO and DMF were used in the reaction (entries 1, 3, 5 and 6). Interestingly, the benzoic acid was formed as the major product when the methyl sulfide was used (entry 7). Presumably, the reducing property of methyl sulfide is not as important as its basicity here. We found that both 2,6-lutidine and $Ph_3P$ are good reagents to decompose the aromatic-substituted ozonide (**6b**) in good yields. However, their products are different.

### III. The comparison of triethylamine and methyl sulfide in reacting with different types of ozonides

From the aforementioned results, we have demonstrated that base treatment is a good choice to workup the ozonolytic reaction involving terminal olefins. It is also interesting to know whether this workup condition is also applicable to the other olefins or not. Since methyl sulfide is the most common reagent to workup the ozonolytic reaction in the literature, we tried to compare the results from these two workups. The triethylamine was used here simply because it is easily available and cheap.

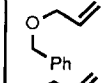
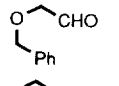
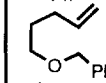
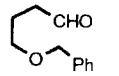
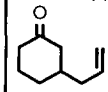
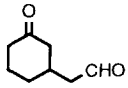
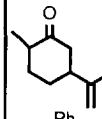
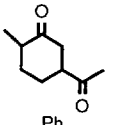
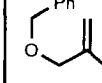
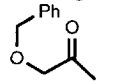
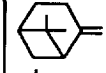
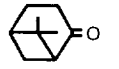
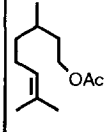
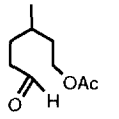
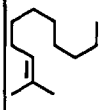
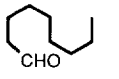
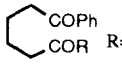
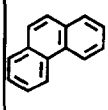
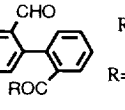
The ozonolysis of the terminal alkenes followed by reacting with 2 molar equivalents of triethylamine gave the corresponding aldehydes in high yields within 4 h (entries 1-3, Table 4). The ozonides derived from 1,1-disubstituted olefins reacted with triethylamine to afford ketones in high yields (entries 4, 5 and 6). In general, the reactions involving methyl sulfide were slower than those of using triethylamine. Some of these reactions were not complete after 40 h or longer and their yields were lower than those obtained from triethylamine treatment.

Ozonolytic cleavage of tri-substituted alkenes was expected to give an acid by use of triethylamine and an aldehyde by use of methyl sulfide. However, we found that aldehydes were obtained in high yields under both reaction conditions. In fact, the ozonolysis of trisubstituted alkenes in dichloromethane gave aldehydes, instead of ozonides, in high yields. Therefore, no reagent was needed to workup this type of ozonolysis (entries 7 and 8).

Ozonolysis of cyclic olefins in dichloromethane produces both monomeric and polymeric ozonides and their ratio is dependent on the ring size and substituents.[12] For example, the ozonolysis of 1-phenylcyclopentene gave the monomeric ozonide in excellent yield (Scheme 1). Both the $Et_3N$ and $Me_2S$ treatments gave different products in high yields (entries 1 and 5, Table 1). However, the ozonolysis of 1-phenylcyclohexene gave predominately the polymeric ozonides and small amount of 6-oxo-6-phenyl-hexanal but no monomeric ozonide. Therefore, the triethylamine treatment gave almost equal amount of a keto-aldehyde (**18b**) and a keto–acid

(**18b'**), whereas the methyl sulfide treatment afforded a keto-aldehyde (**18b**) as the major product in 78% yield (entry 9, Table 4). Similar results and rationale were also applied to the case of the ozonolysis of phenanthrene (entry 10).

**Table 4** Reaction of ozonides derived from alkenes with $Et_3N$ or $Me_2S$

| entry | starting material | product | $Et_3N$ treatment time (h) | $Et_3N$ treatment yield | $Me_2S$ treatment time (h) | $Me_2S$ treatment yield |
|---|---|---|---|---|---|---|
| 1 |  **10a** |  **10b** | 4 | 83% | 20 | 81% |
| 2 |  **11a** |  **11b** | 4 | 80% | 40 | 54% & 38% ozonide **11c** |
| 3 |  **12a** |  **12b** | 3 | 88% | 72 | 54% & 20% ozonide **12c** |
| 4 |  **13a** |  **13b** | 43 | 93% | 72 | 51% & 5% ozonide **13c** |
| 5 |  **14a** |  **14b** | 72 | 64% | 72 | 56% |
| 6 |  **15a** |  **15b** | 8 | 74% | 72 | 23% & 24% ozonide **15c** |
| 7 |  **16a** |  **16b** | — | 90%[a] | — | 90%[a] |
| 8 |  **17a** |  **17b** | — | 93%[a] | — | 93%[a] |
| 9 |  **18a** |  R=H **18b** R=OH **18b'** | 20 | R = H 48% & R = OH 44% | 72 | R = H 78% & R = OH 9% |
| 10 |  **19a** |  R=H **19b** R=OH **19b'** | 48 | R = H 30% & R = OH 42% | 72 | R = H 62% & R = OH 14% |

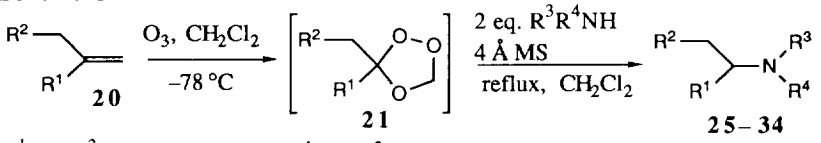
[a] The products were formed after ozonolysis in $CH_2Cl_2$ at -78°C without any reagents.

In most of cases, the extraction technique is good enough to remove the byproducts and get spectroscopically pure product. Convenient workup, low cost, mild reaction conditions, fast reaction rate, and high chemical yield make triethylamine treatment a practical and attractive way to workup the ozonolysis reaction.[13] Another advantage of our method is to avoid using stench methyl sulfide in the ozonolytic reactions.

### IV. The reaction of the ozonides with secondary amine

In the course of extending the scope of the base treatment in the ozonolysis, we found that the reaction of ozonide with tertiary amine and secondary amine gave different products. For example, the mono-substituted ozonide **21a** reacted with piperidine (2.1 mole eq.) to give *N*-3-phenylpropylpiperidine (**25**).[14] Apparently, when the secondary amine was used, the reaction did not stop at 3-phenylpropanal (**22a**) which underwent the further reductive amination. This interesting results prompted us to investigate the reaction carefully and extend the scope of its applications in organic synthesis.

**Scheme 3**




$R^1$=H, $R^2$=$PhCH_2$ **a** $R^1$=H, $R^2$=$PhCH_2$ **a**

$R^1$=$R^2$=$(CH_2)_4$ **b** $R^1$=$R^2$=$(CH_2)_4$ **b**

**Table 5** Formation of the tertiary amines from ozonides and secondary amines

| entry | starting material | product | | yield (%) |
|---|---|---|---|---|
| 1 | $R^1$=H, $R^2$=$PhCH_2$ **20a** | $R^3 = R^4 = -(CH_2)_5-$ | **25** | 85 |
| 2 | $R^1$=H, $R^2$=$PhCH_2$ **20a** | $R^3 = R^4 = -(CH_2CH_2OCH_2CH_2)-$ | **26** | 72 |
| 3 | $R^1$=H, $R^2$=$PhCH_2$ **20a** | $R^3 = R^4 = -(CH_2)_4-$ | **27** | 76 |
| 4 | $R^1$=H, $R^2$=$PhCH_2$ **20a** | $R^3$ = Me, $R^4$ = $CH_2Ph$ | **28** | 81 |
| 5 | $R^1$=H, $R^2$=$PhCH_2$ **20a** | $R^3 = R^4$ = CH(i-Pr)$_2$ | **29** | 83 |
| 6 | $R^1$=$R^2$=$(CH_2)_4$ **20b** | $R^3 = R^4 = -(CH_2CH_2OCH_2CH_2)-$ | **30** | 87 |
| 7 | $R^1$=$R^2$=$(CH_2)_4$ **20b** | $R^3 = R^4 = -(CH_2)_4-$ | **31** | 86 |
| 8 | $R^1$=$R^2$=$(CH_2)_4$ **20b** | $R^3$ = Me, $R^4$ = $CH_2Ph$ | **32** | 79 |
| 9 | $R^1$=$R^2$=$(CH_2)_4$ **20b** | $R^3 = R^4$ = CH(i-Pr)$_2$ | **33** | 0[a] |
| 10 | $R^1$=$R^2$=$(CH_2)_4$ **20b** | $R^3 = R^4 = -(CH_2)_5-$ | **34** | 0[b] |

[a] The cyclohexanone was obtained in 83% yield. [b] The 2-piperidin-1-ylmethyl-cyclohexanone ( **36**) was obtained in 74% yield.

The mono-substituted ozonide **21a** derived from 3-phenyl-1-butene (**20a**) in $CH_2Cl_2$ was treated with piperidine (2.1 mole eq.) in the presence of 4 Å molecular sieves at room temperature and then was heated up to reflux for 10 hr to give the *N*-3-phenylpropylpiperidine (**25**) in 85% yield (Scheme 3 and entry 1, Table 5). The molecule sieves and heating are required to give compound **25** in high yield. Similar result was obtained in high yield when the secondary amine such as morpholine, pyrrolidine, *N*-methyl-*N*-benzylamine or *N*,*N*–diisopropylamine was used (entries 2–5). The plausible mechanism for the formation of the *N*-3-

phenylpropylpiperidine (**25**) was proposed as shown in Figure 1. The first equivalent of the piperidine abstracted the ozonide ring proton from the less hindered side followed by ring fragmentation to give the piperidinium formate (**23a**) and hydrocinnamaldehyde (**22a**).[12b,13] The hydrocinnamaldehyde was then reacted with piperidine in the presence of 4 Å molecular sieves to give the corresponding enamine (**24a**)[15], which was subsequently reduced to the tertiary amine (**3**) by piperidinium formate (**23a**).[16] There are four sequential reactions occurred in the same flask starting from the alkene. The enamine was reduced by formic

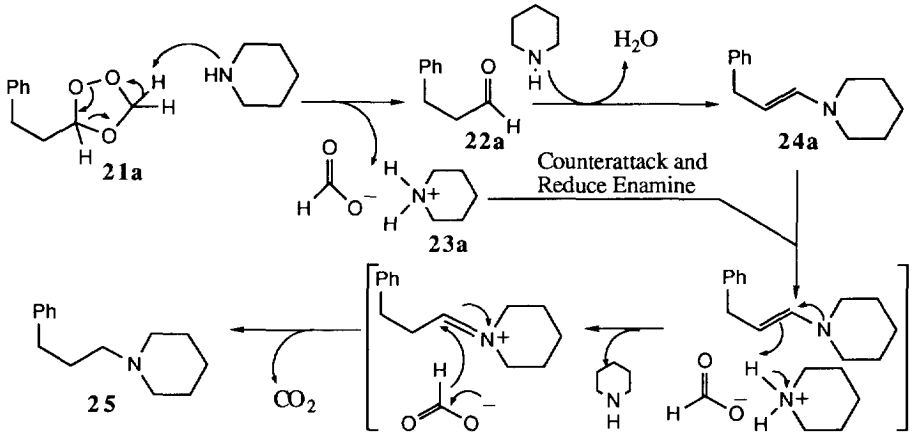
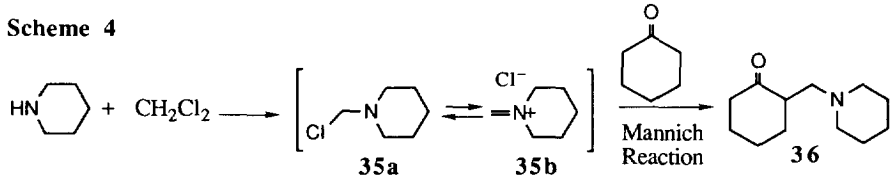
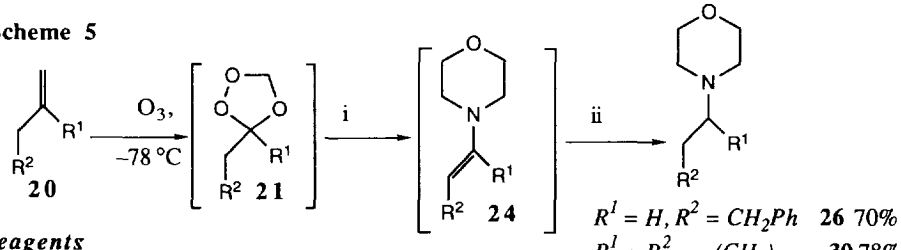



**Figure 1 : The Proposed Mechanism of the Tertiary Amine Formation**

**Scheme 4**




**Scheme 5**




***Reagents***
*(i) Morpholine (2.1 eq.), 4 Å MS, rt, 6 h (ii) $H_2$, 5% Pd/C*

acid to the saturated amine is called the Wallach reaction in which the hydride transfer process was involved. It is possible to use piperidinium formate as a substitute for the Wallach conditions.[16] Besides the reductive amination product, neither the starting carbonyl compound nor its enamine was detected in the crude products. This result indicated that the amount of the piperidinium formate formation is sufficient to reduce the enamine

intermediate. The formation of ammonium formate also strongly supported our E1cb mechanism in the reaction of amine with ozonides described above (Fig.1).

In order to understand whether the 1,1-disubstituted alkenes could also give similar transformation, methylenecyclohexane (**20b**) was demonstrated. The yield of the ozonide formation from methylenecyclohexane is better in *n*-pentane than in $CH_2Cl_2$ at -78 °C.[17] After ozonolysis, *n*-pentane was removed by rotary evaporator at room temperature and redissolved in $CH_2Cl_2$. To the resulting solution was added the morpholine (2.1 mole eq.) and molecular sieves and then was heated up to reflux for 10 h. The *N*-cyclohexylmorpholine (**30**) was formed in good yield (entry 6, Table 5). Similar results were obtained when pyrrolidine, or *N*-methyl-*N*-benzylamine was used (entries 7–8). Their reaction pathway should be similar to the one shown in Figure 1. When *N,N*-diisopropylamine was used, the cyclohexanone instead of tertiary amine was formed as the product in 83% yield (entry 9). Presumably, the enamine formation from *N,N*-diisopropylamine and cyclohexanone is difficult due to the steric hindrance. Although the *N*-cyclohexylmorpholine (**32**) was formed in good yield when morpholine was used (entry 6), there is no *N*-cyclohexylpiperidine (**36**) formation when the piperidine was used (entry 10). To our surprise, the Mannich product (**36**) was isolated in good yield (Entry 10). When the solvent was change from dichloromethane to benzene, cyclohexanone instead of Mannich base was isolated. Clearly, methylene chloride provides an one carbon unit in the final product (**36**) as shown in Scheme 4.[18] It is not clear why the morpholine and piperidine showed so much difference in the present reaction (cf. entries 6 and 10). The enamine formation from piperidine and cyclohexanone is probably not a facile process. The reaction temperature is important to the enamine reduction by ammonium formate. Monitored by TLC, there is little amount of the reductive amination product when the reaction is kept at room temperature. Obviously, the refluxing in $CH_2Cl_2$ is needed to reduce the enamine by the ammonium formate. The enamine intermediates could also be reduced to tertiary amines (**26** and **30**) in high yield by catalytic hydrogenation (Scheme 4).

## CONCLUSIONS

The following conclusions were obtained from this study:

(1) We have clearly demonstrated that the reaction of ozonide with amine- or pyridine-like reagents followed the E1cb mechanism.

(2) Methanolic $K_2CO_3$, Hünig base and triethylamine are useful reagents to convert the mono-substituted aliphatic ozonide to the corresponding aldehyde. Their chemical yields are comparable to that of $Ph_3P$ treatment and are better than that of $Me_2S$ treatment.

(3) The ozonolytic cleavage of alkenes in aprotic solvent followed by treatment with triethylamine provided an alternative way to workup the ozonolysis reaction. It is applicable to the mono-, 1,1-di-, tri-substituted and cyclic olefins. As far as the reaction rate, price, chemical yield and the odor of the reagent were concerned, our method is a good choice to workup the ozonolytic reaction.

(4) The reaction of the ozonides derived from the mono- and 1,1-di-substituted olefins with secondary amines in the presence of 4 Å molecular sieves provided a convenient entry to the corresponding tertiary amine in high yield. This useful transformation involved four sequential reactions in the same flask. The reducing agent (i.e. ammonium formate) in this reductive amination was formed from the reaction of ozonide and amine via E1cb mechanism.

## EXPERIMENTAL

Reagents were used as supplied unless otherwise noted. Reactions were run under dry nitrogen unless otherwise noted. Ozone was prepared with a Fisher ozone generator (Model 501). Silica gel (E. Merck, 230-400 mesh ASTM) was used for flash column chromatography. Melting points were determined using a Yanaco micro melting point apparatus and were uncorrected. The $^{1}H$ and $^{13}C$ NMR spectra were recorded on a Bruker AC 200 and ACP 300 Spectrometer, and chemical shifts were given in ppm downfield from tetramethylsilane (TMS). IR spectra were taken with a Perkin Elmer 882 spectrophotomer and only noteworthy absorptions were listed. Mass spectra were measured on a VG 70-250S mass spectrometer by electronic impact at 70 eV (unless otherwise indicated).

**The general procedure for the ozonolysis of alkene followed by addition of the quenching reagent.**

In a two-neck flask (25 mL), equipped with a magnetic stirrer, a drying tube and a gas dispersion tube (with porous fritted tip), were placed 10 mL of dichloromethane and alkene (2 mmol). A stream of ozone was bubbled through the solution at -78 °C. Ozone treatment was terminated when the solutions assumed a blue color. Excess ozone was removed by a stream of nitrogen. The quenching reagent (*i.e.* 4 mmol of $Et_3N$, 10 mmol of $Me_2S$, or inorganic base whose amount of use was indicated in Table 1) was then added to the solution, which was warmed up to room temperature. The reaction time and chemical yields were shown in Tables 1, 2, and 3, respectively. The workup procedures were dependent on the reagents used as described in the following.

**(a) When $Et_3N$ was used as quenching reagent**

The reaction mixture was concentrated under reduced pressure. The residue was chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired carbonyl product. If the desired product is a carboxylic acid, the reaction mixture was acidified with 5% HCl. The extracts were washed with water and brine. The organic phase was dried ($Na_2SO_4$), filtered, concentrated, and chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired carboxylic acid.

**(b) When $Me_2S$ was used as quenching reagent**

The reaction mixture was concentrated under reduced pressure in a well-ventilated hood. The residue was chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired product.

**(c) When KOBu-t or NaH was used as quenching reagent**

To 10 mL of dichloromethane solution of ozonide was added 10 mL of THF as cosolvent. The KOBu-t (or NaH) was added to the ozonide solution and stirred at 0 °C. When the reaction completed, the reaction mixture was acidified with 5% HCl and extracted with dichloromethane. The extracts were washed with water and brine. The organic layer was dried ($Na_2SO_4$), filtered, concentrated, and chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired product.

**(d) When LiOH or $K_2CO_3$ was used as quenching reagent**

To the ozonide solution was added LiOH in 50% aqueous THF ( or 10 mL of MeOH and $K_2CO_3$) at 0 °C. When the reaction completed, the reaction mixture was acidified carefully with 5% HCl and extracted with dichloromethane. The extracts were washed with water and brine. The organic phase was dried ($Na_2SO_4$),

filtered, concentrated, and chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired product.

**The general procedure for the ozonolysis of styrene followed by addition of a quenching reagent.**

The ozonide obtained from styrene was prepared at –78°C in pentane in 75% yield.[11] After ozonation, the solvent was removed by rotary evaporator. The residue was purified by flash column chromatography. The purified ozonides were then reacted with a variety of reagents in dichloromethane at room temperature. When the reaction completed, the reaction mixture was acidified with 5% HCl and extracted with dichloromethane. The extracts were washed with water and brine. The organic phase was dried ($Na_2SO_4$), filtered, concentrated. It is difficult to purify the benzaldehyde by column chromatography due to its instability in silica gel. Therefore, the crude products were treated with $CH_2N_2$ to give a mixture of benzaldehyde and methyl benzoate. The chemical yield and product ratio in Table 3 were then determined by gas chromatography with hexadecane as the internal standard.

***1-Phenyl-6,7,8-trioxa-bicyclo[3.2.1]octane (2)***: colorless oil; IR (neat) (ν, $cm^{-1}$): 3090, 3063, 3037, 2963, 2928, 1477, 1351, 1331, 1254, 1130, 1103, 1068, 1042, 937, 907 (O-O); $^1H$ NMR ($CDCl_3$) δ 1.71–2.41 (m, 6H), 5.93 (s, 1H), 7.31–7.56 (m, 5H); $^{13}C$ NMR ($CDCl_3$) δ 15.9, 28.9, 33.0, 103.5, 107.8, 125.6, 128.2, 129.2, 137.8; MS (m/z): 192 ($M^+$, 1), 176 (1), 160 (18), 148 (8), 132 (2), 122 (19), 105 (100), 87 (15), 77 (51), 71 (67); HRMS (m/z): 192.0782 ($M^+$, $C_{11}H_{12}O_3$, calcd 192.0786).

***5-Oxo-5-phenyl-pentanal (3)***: pale yellow liquid; IR (neat) (ν, $cm^{-1}$): 3059, 2942, 2897, 2829, 2729, 1719 (HC=O), 1675 (PhC=O), 1596, 1442, 1365, 1226, 1177, 999, 966; $^1H$ NMR ($CDCl_3$) δ 2.05 (m, 2H), 2.57 (td, $J$ = 0.9 and 7.1 Hz, 2H), 3.03 (t, $J$ = 7.0 Hz, 2H), 7.39–7.97 (m, 5H), 9.78 (s, 1H, CHO) ; $^{13}C$ NMR ($CDCl_3$) δ 16.3, 37.1, 42.8, 127.8, 128.4, 132.9, 136.5, 199.1 (PhC=O), 201.8 (HC=O); MS (m/z): 176 ($M^+$, 3), 158 (8), 148 (18), 120 (20), 105 (100), 91 (3), 77 (45); HRMS (m/z): 176.0842 ($M^+$, $C_{11}H_{12}O_2$, calcd 176.0837).

***5-Oxo-5-phenyl-pentanoic acid (4)*** : white solid, m.p. 123–125 °C; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 2400–3500 (br, -OH), 1706 (C=O), 1686 (PhC=O), 1256, 1244; $^1H$ NMR ($CDCl_3$) δ 2.09 (m, 2H), 2.51 (t, $J$ = 7.0 Hz, 2H), 3.08 (t, $J$ = 7.0 Hz, 2H), 7.26–7.98 (m, 5H); $^{13}C$ NMR ($CDCl_3$) δ 19.0, 33.0, 37.3, 128.0, 128.6, 133.1, 136.7, 178.8 (COOH), 199.4 (PhC=O); MS (m/z): 192, ($M^+$, 25), 156 (56), 139 (40), 129 (17), 114 (35), 105 (100), 77 (39), 72 (40); HRMS (m/z): 192.0782 ($M^+$, $C_{11}H_{12}O_3$, calcd 192.0786).

***(E)-2-n-Heptyl-undeca-2-enal (8a)*** : colorless oil; IR (neat) (ν, $cm^{-1}$): 2929, 1676 (C=O), 1099 ; $^1H$ NMR ($CDCl_3$) δ 0.84-0.91 (m, 6H), 1.25-1.54 (m, 22H), 2.23 (br t, $J$ = 7.3 Hz, 2H), 2.35 (q, $J$ = 7.3 Hz, 2H), 6.43 (t, $J$ = 7.4 Hz, 1H), 9.35 (s, 1H); $^{13}C$ NMR ($CDCl_3$) δ 14.02, 22.61, 24.00, 28.71, 28.89, 29.10, 29.35, 29.61, 31.79, 143.83 (C=C), 155.20 (C=C), 195.22 (C=O); MS (m/z): 266 ($M^+$, 40), 209 (10), 181 (35), 167 (35), 153 (48), 135 (62), 109 (34), 91 (100), 81 (68), 69 (88); HRMS (m/z): 266.2617 ($M^+$, $C_{18}H_{34}O$, calcd 266.2610).

***Benzyloxy-acetaldehyde (10b)*** : colorless oil; IR (neat) (ν, $cm^{-1}$): 3451, 3067, 3032, 2913, 2866, 2825, 2247, 1732 (C=O), 1449, 1386, 1246, 1204, 1107, 1025, 891; $^1H$ NMR ($CDCl_3$) δ 4.08 (s, 2H), 4.61 (s, 2H), 7.29–7.37 (m, 5H), 9.69 (t, $J$ = 0.6 Hz, 1H); MS (m/z): 150 ($M^+$, 2), 129 (1), 121 (4), 107 (47), 91 (100), 77 (10), 65 (20); HRMS (m/z): 150.0668 ($M^+$, $C_9H_{10}O_2$, calcd 150.0681).

***4-Benzyloxy-butyraldehyde (11b)*** : colorless oil; IR (neat) (ν, $cm^{-1}$): 3488, 3239, 3205, 3078, 3053, 2991, 2944, 1707 (C=O); $^1H$ NMR ($CDCl_3$) δ 1.94 (m, 2H), 2.54 (td, $J$ = 1.6 and 7.1 Hz, 2H); 3.05 (t, $J$ = 6.1 Hz, 2H); 4.48 (s, 2H), 7.25-7.40 (m, 5H, Ph-H), 9.77 (t, $J$ = 1.5 Hz, 1H); $^{13}C$ NMR ($CDCl_3$) δ 22.5, 40.9, 69.1, 72.9, 127.6, 128.4, 138.2, 202.3; MS (m/z): 178 ($M^+$, 4), 150 (5), 134 (2), 123 (2), 107 (33), 91 (100), 77 (15), 71 (10), 65 (15); HRMS (m/z): 178.0986 ($M^+$, $C_{11}H_{14}O_2$, calcd 178.0994).

***3-(3-Benzyloxy-propyl)-[1.2.4]-trioxolane (11c)*** : colorless oil; $^1H$ NMR ($CDCl_3$) δ 1.80 (m, 4H), 3.51 (t, $J$ = 5.8 Hz, 2H), 4.51 (s, 2H), 5.04 (s, 1H), 5.18 (s, 2H), 7.33 (m, 5H); $^{13}C$ NMR ($CDCl_3$) δ 24.0, 28.1, 69.5, 72.8, 94.0, 103.5, 127.5, 128.3, 138.3.

***(3-Oxo-cyclohexyl)-acetaldehyde (12b)*** : colorless oil; IR (neat) (ν, $cm^{-1}$): 2939, 1704 (C=O), 1224, 724; $^1H$ NMR ($CDCl_3$) δ 1.23–2.56 (m, 11H), 9.79 (s, 1H); $^{13}C$ NMR ($CDCl_3$) δ 24.9, 31.0, 33.2, 34.9, 39.4, 41.1, 47.5, 49.9, 200.6 (HC=O), 210.2 (C=O); MS (m/z): 140 ($M^+$, 33), 120 (94), 105 (26), 97 (100), 91 (85), 84 (72), 77 (25), 69 (82), 65 (26); HRMS (m/z): 140.0810 ($M^+$, $C_8H_{12}O_2$, calcd 140.0837).

***3-[1.2.4]Trioxolan-3-ylmethyl-cyclohexanone (12c)*** : colorless oil; IR (neat) (ν, $cm^{-1}$): 2941, 1701, 1448, 1431, 1400, 1381, 1348, 1313, 1286, 1229, 1203, 1183, 1101, 1059; $^1H$ NMR ($CDCl_3$) δ 1.40–2.30 (m, 11H), 5.04 (s, 1H), 5.18 (s, 1H), 5.19 (t, $J$ = 5.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$) δ 24.6, 30.9, <u>31.0</u>, 34.5, 37.3, 40.7, 47.5, <u>47.6</u>, 93.6, 101.9, 201.0; MS (m/z): 156 ($M^+$-30), 139, 112, 97 (100), 95, 84, 69, 58, 55; HRMS (m/z): 156.0758 ($M^+$-$CH_2O$, $C_8H_{12}O_3$, calcd 156.0786). Underline imply the absorptions from diastereomer.

***5-Acetyl-2-methyl-cyclohexanone (13b)*** : colorless oil; IR (neat) (ν, $cm^{-1}$): 2972, 2936, 2869, 1699 (C=O), 1356, 1239, 1164; $^1H$ NMR ($CDCl_3$) δ 1.03 (d, $J$ = 6.5 Hz, 3H), 1.15–2.92 (m, 11H); $^{13}C$ NMR ($CDCl_3$) δ 14.2, 27.8, 28.2, 34.5, 42.7, 44.6, 52.1, 208.2 (C=O), 211.4 (C=O); MS (m/z): 154 ($M^+$, 23), 139 (2), 121 (2), 111 (100), 97 (12), 83 (20), 71 (11).

***2-Methyl-5-(3-methyl-[1.2.4]trioxolan-3-yl)-cyclohexanone (13c)*** : colorless oil; IR (neat) (ν, $cm^{-1}$): 2968, 2935, 1705 (C=O), 1374, 1212, 1132, 1102, 1058, 964, 904; $^1H$ NMR ($CDCl_3$) δ 1.03 (d, $J$ = 6.4 Hz, 3H), 1.36–2.55 (m, 11H), 5.11 (d, $J$ = 15.3 Hz, 2H); $^{13}C$ NMR ($CDCl_3$) δ 14.2, 20.0, <u>20.4</u>, <u>26.1</u>, 26.4, 34.0, 42.4, 42.6, 44.6, 46.3, <u>94.0</u>, 94.1, 109.8, 211.4 (C=O). Underline imply the absorptions from diastereomer.

***1-Benzyloxy-propan-2-one (14b)*** : colorless; IR (neat) (ν, $cm^{-1}$): 2924, 2866, 2250, 1718 (C=O), 1418, 1355, 1262, 1108, 1023; $^1H$ NMR ($CDCl_3$) δ 2.14 (s, 3H), 4.05 (s, 2H), 4.58 (s, 2H), 7.31–7.38 (m, 5H); $^{13}C$ NMR ($CDCl_3$) δ 26.2, 73.1, 75.1, 127.7, 127.8, 128.3, 137.0, 206.5; MS (m/z) : 165 ($M^+$+1, 1), 163 ($M^+$-1, 1), 148 (2), 135 (1), 121 (1), 107 (60), 105 (11), 91 (100), 77 (10), 65 (20).

***7,7-Dimethyl-bicyclo[3.1.1]heptan-2-one (15b)*** : colorless oil; $^1H$ NMR ($CDCl_3$) δ 0.86 (s, 3H), 1.33 (s, 3H), 1.58 (d, $J$ = 9.7 Hz, 1H), 1.64–2.68 (m, 7H); $^{13}C$ NMR ($CDCl_3$) δ 21.3, 22.0, 25.1, 25.8, 32.6, 40.3, 57.8, 214.7 (C=O).

***β-Pinene ozonide (<u>15c</u>)*** : colorless oil; $^1H$ NMR ($CDCl_3$) δ 0.93 (s, 3H), 1.23 (s, 3H), 1.42 (d, $J$ = 10.6 Hz, 1H), 1.85–2.35 (m, 7H), 4.99 (s, 1H), 5.07 (s, 1H); $^{13}C$ NMR ($CDCl_3$) δ 22.4,.22.8, 26.2, 26.4, 27.7, 40.0, 49.1, 92.9.

***6-Acetoxy-4-methylhexanal (16b)*** : colorless oil; IR (neat) (ν, $cm^{-1}$): 2963, 2931, 1720, 1365, 1231, 1054 ; $^1H$ NMR ($CDCl_3$) δ 0.93 (d, $J$ = 6.3 Hz, 3H), 1.40–1.71 (m, 5H), 2.05 (s, 3H, OAc), 2.43-2.49 (m, 2H), 4.05-4.15 (m, 2H), 9.78 (t, $J$ = 1.9 Hz, 1H); $^{13}C$ NMR ($CDCl_3$) δ 19.0, 20.9, 28.6, 29.4, 35.1, 41.4, 62.5, 171.1 (C=O), 202.3 (C=O).

***6-Oxo-6-phenyl-hexanal (18b)*** : colorless oil; IR (neat) (ν, $cm^{-1}$): 2950, 1720 (C=O), 1682, 1440, 1356, 1221, 1075, 714; $^1H$ NMR ($CDCl_3$) δ 1.76 (m, 4H), 2.50 (td, *J* = 1.5 Hz and 6.9 Hz, 2H), 3.00 (t, *J* = 6.8 Hz, 2H), 7.40 –7.60 (m, 3H), 7.92–7.98 (m, 2H), 9.77 (t, *J* =1.5 Hz, 1H); $^{13}C$ NMR ($CDCl_3$) δ 21.6, 23.5, 38.0, 43.6, 127.8, 128.5, 132.9, 135.7, 199.6 (PhCO), 202.2 (CHO); MS (m/z): 190 ($M^+$, 2), 172 (2), 162 (4), 146 (10), 133 (5), 120 (46), 105 (100), 77 (36); HRMS (m/z): 190.0999 ($M^+$, $C_{12}H_{14}O_2$, calcd 190.0994).

***6-Oxo-6-phenyl-hexanoic acid (18b')*** : white solid, m.p. 66-68 °C; IR (neat) (ν, $cm^{-1}$): 2500-3600 (br, OH), 1705 (C=O), 1682 (PhCO), 1443, 1407, 1254, 1220; $^1H$ NMR ($CDCl_3$) δ 1.40–2.30 (m, 4H), 2.43 (t, J = 6.7 Hz, 2H), 3.01 (t, J = 6.8 Hz, 2H), 7.26-7.61 (m, 3H), 7.92-7.98 (m, 2H); $^{13}C$ NMR ($CDCl_3$) δ 23.5, 24.3, 33.8, 38.1, 128.0, 128.6, 133.0, 136.9, 179.3 (C=O), 199.9 (PhC=O).

***Biphenyl-2,2'-dicarbaldehyde (19b)*** : pale yellow solid, m.p. 51–53 °C; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 3036, 2851, 2755, 1689 (C=O), 1648, 1595, 1391, 1246, 1194, 1104, 821; $^1H$ NMR ($CDCl_3$) δ 7.36 (dd, *J* = 1.1 and 6.1 Hz, 2H), 7.56-7.72 (m, 4H), 8.06 (dd, *J* = 1.7 and 7.0 Hz, 2H), 9.83 (d, *J* = 0.6 Hz, 2H); $^{13}C$ NMR ($CDCl_3$) δ 128.5, 128.7, 131.6, 133.4, 134.5, 141.2, 191.0 (C=O); MS (m/z): 210 ($M^+$, 20), 181 (100), 152 (61), 135 (10), 120 (16), 105 (36), 91 (8), 77 (16); HRMS (m/z): 210.0681 ($M^+$, $C_{14}H_{10}O_2$, calcd 210.0688).

***2'-Formyl-biphenyl-2-carboxylic acid (19b')*** : yellow solid, m.p. 114-116°C; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 2500–3600 (br, -OH), 1690 (C=O), 1597, 1398, 1285, 726; $^1H$ NMR ($CDCl_3$) δ 7.16–8.11 (m, 8H), 9.71 (s, 1H); $^{13}C$ NMR ($CDCl_3$) δ 128.3, 127.6, 128.1, 130.0, 130.2, 130.8, 131.8, 133.0, 133.6, 139.5, 171.4 (COOH), 191.6 (CHO); MS (m/z): 181 ($M^+$-45, 3), 149 (3), 119 (8), 115 (8), 84 (100), 72 (1); HRMS (m/z): 181.0649 ($M^+$-$CO_2H$, $C_{13}H_9O$, calcd 181.0653).

**Typical procedure for reactions of ozonides with secondary amine in the presence of 4Å molecular sieves.**

In a 25 mL two-neck flask, equipped with a magnetic stirrer, a drying tube and a gas dispersion tube (with porous fritted tip), were placed 8 mL of dichloromethane and 4-phenyl-1-butene (**20a**) (132.2 mg, 1 mmol). A stream of ozone was bubbled through the solution at - 78 °C. Ozone treatment was terminated when the solutions assumed a blue color. Excess ozone was removed by a stream of nitrogen. The reaction mixtures were then allowed to warm up to room temperature. To the resulted mixtures were added 4 Å molecular sieves (1.3 g) and piperidine (425.1 mg, 2 mmol) in 2 mL of dichloromethane. The reaction was refluxed for 12 h. The molecular sieves were removed by passing through the Celite. The filtrate was concentrated and chromatographed on a silica gel column by elution with EtOAc/hexane (1/1) to give *N*-(3-phenylpropyl)piperidine (**27**) (172.7 mg, 85% yield) as a colorless oil. The reactions with other secondary amines are listed in Table 5.

***N-(3-Phenylpropyl)piperidine (25)***: Pale yellow oil; $^1H$-NMR ($CDCl_3$) δ 1.30–1.70 (m, 6H), 1.79–1.91 (m, 2H), 2.31–2.39 (m, 6H), 2.61 (t, *J* = 7.7 Hz, 2H, Ar-$CH_2$), 7.14–7.29 (m, 5H, Ar-H); $^{13}C$-NMR (CDCl3) δ 24.19, 25.62, 28.26, 33.67, 54.34, 58.61, 125.56, 128.11, 128.20, 141.95; IR ($CH_2Cl_2$) (ν, cm $^{-1}$): 1657, 1518, 1253, 1116, 904, 707; MS (m/z): 203 ($M^+$, 8), 98 (100), 91 (12), 77 (5); HRMS (m/z): 203.1667 ($M^+$, $C_{14}H_{21}N$, Calcd 203.1674).

***N-(3-Phenylpropyl)morpholine (26)***: Pale yellow oil; $^1H$-NMR ($CDCl_3$) δ 1.77-1.89 (m, 2H), 2.36-2.44 (m, 6H), 2.61-2.72 (m, 2H), 3.66-3.73 (m, 4H), 7.16-7.27 (m, 5H); $^{13}C$-NMR ($CDCl_3$) δ 28.16,

33.51, 53.64, 58.28, 66.93, 125.69, 128.29, 141.98; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 2945, 2860, 2811, 1601, 1255, 1112, 1069; MS (m/z) (33 eV): 205 ($M^+$, 12), 117 (8), 100 (100), 91 (10); HRMS (m/z): 205.1469 ($M^+$, $C_{13}H_{19}NO$, Calcd 205.1467).

***N-(3-Phenylpropyl)pyrrolidine (27)***: Pale yellow oil; $^1$H-NMR ($CDCl_3$) δ 1.88-2.04 (m, 6H), 2.64-2.83 (m, 8H), 7.17-7.28 (m, 5H); $^{13}$C-NMR ($CDCl_3$) δ 23.27, 29.98, 33.62, 53.94, 55.75, 125.68, 128.22, 141.70; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 2959, 1099, 718; MS (m/z) (33 eV): 189 ($M^+$, 10), 91 (9), 84 (100); HRMS (m/z): 189.1516 ($M^+$, $C_{13}H_{19}N$, Calcd 189.1517).

***N-(3-Phenylpropyl)-N-methylbenzylamine (28)***: Pale yellow oil; $^1$H-NMR ($CDCl_3$) δ 1.84 (m, 2H), 2.18 (s, 3H), 2.42 (t, $J$ = 7.3 Hz, 2H), 2.64 (t, $J$ = 7.6 Hz, 2H), 3.48 (s, 2H), 7.16-7.31 (m, 10H); $^{13}$C-NMR ($CDCl_3$) δ 29.14, 33.54, 42.11, 56.83, 62.23, 125.64, 126.85, 128.15, 128.22, 128.39, 129.01, 139.15, 142.38; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 2945, 1605, 1446, 1253, 1114, 1074, 1024; MS (m/z) (55 eV): 239 ($M^+$, 11), 134 (100), 114 (10), 91 (95); HRMS (m/z): 239.1671 ($M^+$, $C_{17}H_{21}N$, Calcd 239.1674).

***N,N-Diisopropyl-3-phenylpropylamine (29)***: Pale yellow oil; $^1$H-NMR ($CDCl_3$) δ 0.99 (d, $J$ = 6.6 Hz, 12H), 1.66-1.81 (m, 2H), 2.43 (t, $J$ = 7.6 Hz, 2H), 2.59 (t, $J$ = 7.8 Hz, 2H), 2.85-3.07 (m, 2H), 7.11-7.26 (m, 5H); $^{13}$C-NMR ($CDCl_3$) δ 20.64, 32.82, 33.70, 44.94, 48.54, 125.51, 128.19, 128.34, 142.69; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 3051, 2966, 2869, 1600, 1418, 1360, 1252, 1200, 1156, 1112; MS (m/z) (33 eV): 219 ($M^+$, 15), 204 (52), 114 (100), 100 (10), 84 (58), 72 (27); HRMS (m/z): 219.1395 ($M^+$, $C_{15}H_{25}N$, Calcd 219.1387).

***N-Cyclohexylmorpholine (30)***: Pale yellow oil; $^1$H-NMR ($CDCl_3$) δ 1.05-1.45 (m, 5H), 1.55-2.10 (m, 5H), 2.12-2.30 (m, 1H), 2.56-2.62 (m, 4H), 3.71-3.77 (m, 4H); $^{13}$C-NMR ($CDCl_3$) δ 25.58, 26.12, 28.61, 49.46, 63.68, 67.14; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 2932, 1442, 1114, 1067; MS (m/z): 169 ($M^+$, 21), 126 (100), 84 (98); HRMS (m/z): 169.1461 ($M^+$, $C_{10}H_{19}NO$, Calcd 169.1467).

***N-Cyclohexylpyrrolidine (31)***: Pale yellow oil; $^1$H-NMR ($CDCl_3$) δ 1.12-1.95 (m, 10H), 2.04-2.16 (m, 4H), 2.80-3.02 (m, 1H), 3.18-3.35 (m, 4H); $^{13}$C-NMR ($CDCl_3$) δ 22.91, 24.32, 28.40, 50.55, 63.95, 77.00; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 2939, 2860, 1605, 1449, 1280, 1114, 795; MS (m/z): 153 ($M^+$, 23), 124 (5), 110 (92), 97 (12), 84 (100); HRMS (m/z): 153.1519 ($M^+$, $C_{10}H_{19}N$, Calcd 153.1517).

***N-Cyclohexyl-N-methylbenzylamine (32)***: Pale yellow oil; $^1$H-NMR ($CDCl_3$) δ 1.10-1.39 (m, 5H), 1.55-1.65 (m, 1H), 1.78-1.90 (m, 4H), 2.18 (s, 3H), 2.37-2.46 (m, 1H), 3.54 (s, 2H), 7.20-7.33 (m, 5H); $^{13}$C-NMR ($CDCl_3$) δ 25.98, 26.40, 28.68, 37.61, 57.80, 62.48, 126.55, 128.06, 128.70, 140.38; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 2932, 2855, 2789, 1445, 1107, 905, 719; MS (m/z) (33 eV): 203 ($M^+$, 33), 160 (100), 146 (12), 91 (60), 84 (21); HRMS (m/z): 203.1677($M^+$, $C_{14}H_{21}N$, Calcd 203.1674).

***2-Piperidin-1-ylmethyl-cyclohexanone (36)***: Pale yellow oil; $^1$H-NMR ($CDCl_3$) δ 1.43-1.73 (m, 12H), 2.25 (dd, $J$ = 6.8 and 12.7 Hz, 1H), 2.20-2.60 (m, 7H), 2.86 (dd, $J$ = 5.7 and 12.5 Hz, 1H); $^{13}$C-NMR ($CDCl_3$) δ 24.17, 24.55, 25.75, 27.98, 32.98, 41.90, 48.52, 54.74, 58.07, 212.67; IR ($CH_2Cl_2$) (ν, $cm^{-1}$): 2939, 1702 (C=O), 1120; MS (m/z): 195 ($M^+$, 2), 110 (12), 98 (100), 84 (22), 67 (32); HRMS (m/z): 195.1621($M^+$, $C_{12}H_{21}NO$, Calcd 195.1623).

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## REFERENCES AND NOTES


1. (a) Hon, Y. S.; Lu, L.; Li, S. Y. *J. Chem. Soc., Chem. Commun.* **1990**, 1627. (b) Hon, Y. S.; Chu, K. P.; Hong, P. C.; Lu, L. *Synth. Commun.* **1992**, *22*, 429. (c) Hon, Y. S.; Lu, L.; Chang, R. C.; Chu, K. P.; Lin, S. W. *Chin. J. Org. Chem. (Youji Huaxue)* **1993**, *13*, 286.
2. (a) Lorenz, O.; Parks, C. R. *J. Org. Chem.* **1976**, *30*, 1977. (b) Knowles, W. S.; Thompson, Q. E. *J. Org. Chem.* **1960**, *25*, 1031. (c) Carles, J.; Fliszar, S. *Can. J. Chem.* **1972**, *51*, 2552 and references cited therein. (d) Pappas, J. J.; Keaveney, W. P. *Tetrahedron Lett.* **1966**, *7*, 4273. (e) Bailey, P. S. in *Ozonation in Organic Chemistry*, Academic Press, New York, 1978, Vol. 1, Chapter 8.
3. (a) Isobe, M.; Iio, H.; Kawai, T.; Goto, T. *Tetrahedron Lett.* **1977**, *18*, 703. (b) Ferezou, J. P.; Julia, M.; Khourzom, R.; Pancraazi, A.; Robert, P. *Synlett* **1991**, 611. (c) Colvin, E. W.; Cameron, S. *J. Chem. Soc., Chem. Commun.* **1986**, 1084. (d) Hashimoto, H.; Furuichi, K.; Miwa, T. *J. Chem. Soc., Chem. Commun.* **1987**, 1002. (e) Bertozzi, C. R.; Bednarski, M. D. *Tetrahedron Lett.* **1992**, *33*, 3109.
4. (a) Razumovskii, S. D.; Zaikov, G. E. *Ozone and its Reactions with Organic Compounds*, Chapter 9, p 370, Elsevier, Netherlands, 1984. (b) Pobedimskii, D. G.; Razumovskii, S. D. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1970**, *3*, 602; *Chem. Abst.* **1970**, *73*,13853n.
5. Ellam, R. M.; Padbury, J. M. *J. Chem. Soc., Chem. Commun.* **1972**, 1086.
6. Garbisch, W. W. Jr. *J. Org. Chem.* **1961**, *26*, 4165.
7. The retention time for pyridine *N*-oxide in DB$^{TM}$-17 GC column (30 m x 0.32 mm I.D., 1.00 mm film thick) is 31.57 minute. The oven temperature is ranged at 80°C – 210 °C at 2 °C/min and nitrogen is the carrier gas (the total flow rate is 181.4 mL/sec). The authentic sample of pyridine *N*-oxide was purchased from Aldrich Chemical Company, U.S.A..
8. Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*, 3rd Ed., Chapter 6, Part A, Plenum Press, New York, N.Y., 1990.
9. Tanner, D. D.; Yang, C. M. *J. Org. Chem.* **1993**, *58*, 5907.
10. Hon, Y. S.; Lu, L.; Chang, R. C.; Chu, K. P. *Heterocycles* **1991**, *32*, 437.
11. Criegee, R.; Korber, H. *Adv. Chem. Ser.* **1972**, *112*, 23.
12. (a) Bailey, P. S. in *Ozonation in Organic Chemistry*, Academic Press, New York, 1978, Vol. 1, Chapter 5, p 33. (b) Hon, Y. S.; Yan, J. L. *Tetrahedron Lett.* **1993**, *34*, 6591.
13. Hon, Y. S.; Lin, S. W.; Chen, Y. J. *Synth. Commun.* **1993**, *23*, 1543.
14. Hon, Y. S.; Lu, L. *Tetrahedron Lett.* **1993**, *34*, 5309.
15. (a) Cook, A. G. *Enamines : Synthesis, Structure, and Reactions*, Marcel Dekker, Inc., New York, New York, U.S.A., 1988. (b) Hickmott, P. W. *Tetrahedron* **1982**, *38*, 1975. (c) Hickmott, P. W. *Tetrahedron* **1982**, *38*, 3363.
16. (a) Lukes, R.; Jizba, J. *Chem. Listy* **1953**, *47*, 1336. (b) Leonard, N. J.; Sauers, R. R. *J. Am. Chem. Soc.* 1957, **79**, 6210. (c) Moore, M. L. *Org. React.* **1949**, *5*, 301. (d) Noyce, D. S.; Bachelor, F. W. *J. Am. Chem. Soc.* **1952**, *74*, 4577. (e) Lukasiewicz, A. *Tetrahedron* **1963**, *19*, 1789. (f) Awachie, P. I.; Agwada, V. C. *Tetrahedron* **1990**, *46*, 1899.

17. Besides the ozonide, cyclohexanone was also formed in 14% yield when methylenecyclohexane was ozonized in $CH_2Cl_2$ at -78 °C. However, the formation of cyclohexanone was suppressed to minimum (8%) when the solvent was changed from $CH_2Cl_2$ to *n*-pentane.
18. (a) Hon, Y. S.; Chang, F. J.; Lu, L. *J. Chem. Soc., Chem. Commun.* **1994**, 2041. (b) Matsumoto, K. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 922. (c) Matsumoto, K.; Hashimoto, S.; Ikemi, Y.; Otani, S. *Heterocycles* **1984**, *22*, 1417. (d) Souquet, F.; Martens, T.; Fleury, M. B. *Synth. Commun.* **1993**, *23*, 817.

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