# AMINO SUBSTITUENT EFFECT ON OXYGENATION OF ENAMINES CATALYZED BY CUPRIC CHLORIDE

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In the cupric chloride-catalyzed oxygenation of isobutyraldehyde
enamines and cyclohexanone enamines of various secondary amines,
the amino substituent remarkably affects the reactivity and the
relative rates correlate well with their 1st ionization potentials.

Oxygenation of enamines with transition metal catalysts[1] has been a focus of considerable attention in view of the similarity of its product pattern to that of photo-oxygenation.[2] But the mechanism of this catalytic reaction still remains uncertain. In the course of our study on the copper-catalyzed oxygenation of amino compounds,[3] we examined the catalytic oxygenation of air stable enamines having various amino substituents, and found that the relative rates correlate well with their ionization potentials. From the linearity of the correlation and the preliminary kinetic study, a non-chain mechanism involving the coordinative activation of both enamine and molecular oxygen is proposed.

Two series of enamines were chosen as the substrate; one series is 1-amino substituted 2-methyl propenes (Ia)∿(Ie) and the other is 1-amino substituted 1-cyclohexenes (IIa)∿(IIc). In both series amino substituent was systematically changed. The oxygenation of these enamines with cupric chloride easily proceeded without any induction period[4] in aprotic solvent, e.g. chloroform, dimethylformamide, or acetonitrile. In the case of type-(I) enamines, double bond cleavage products, acetone and the corresponding formamide (IIIa)∿(IIIe), were

Scheme 1.
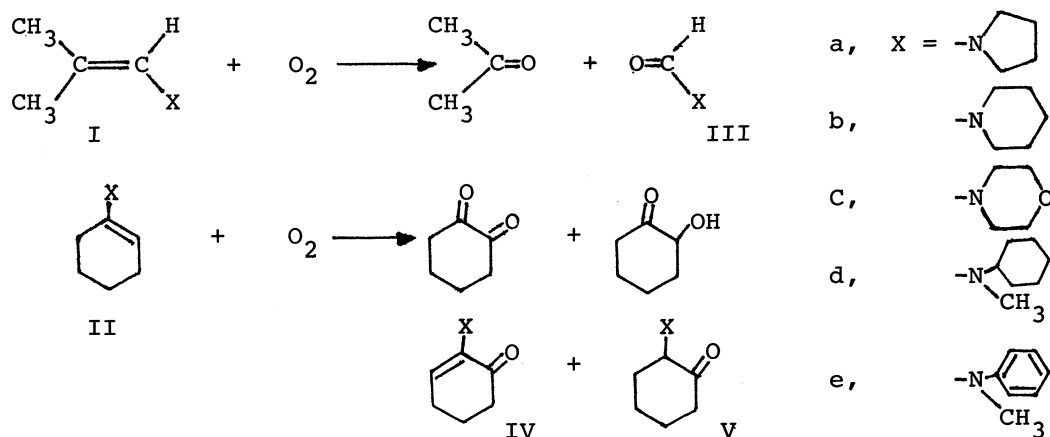
obtained in high to quantitative yields, while the reaction of type-(II) enamines
gave four major products in modest to low yields, cyclohexane dione (25∿32%), α-
hydroxy cyclohexanone (8∿15%), enaminoketone (IVa)∿(IVc) (5∿18%) and aminoketone[5]
(Va)∿(Vc) (4∿7%), respectively. Thus the similarity of product pattern between
this reaction and the photo-reaction[2] suggests the interception of a common
intermediate, 1,2-dioxetane, in both reactions.

An especially interesting aspect of the oxygenation of these enamines is the
remarkable effect of amino substituent on the relative rate. That is, the reac-
tion of (Ie) was twenty fold faster than that of (Ic). In order to understand this
substituent effect, it may be essential to find the main structural factor concern-
ing the relative reactivity of these enamines. As one of such factors, we adopted
the oxidation potential, which can be represented by the ionization potential
(IP).[6] IP's of these enamines were newly measured by He-I photo-electron spectro-
scopy.[7] Oxygen absorption rate (V) at the beginning of the reaction was measured
with the usual gas burette apparatus.[8] Table 1 shows the physical data and the
relative rates of oxygenation. There is a fairly good correlation between these
relative rates and 1st IP's in each series of enamines, (Ia)∿(Ie) and (IIa)∿(IIc),
as shown in Fig 1. The deviation of (Ie) from the linearity may be attributed to
the rather different nature of 1st IP level from that of other enamines.[9]

Table 1. Comparison of the ionization potentials and the relative rates
of $CuCl_2$-catalyzed oxygenation of various enamines

| Substrate | π-Ionization potential[a] (eV) | | | Relative rate of oxygenation[b] ($V/V^s$) |
|---|---|---|---|---|
| | $IP_1$ | $IP_2$ | Others | |
| Ia | 7.79 | 8.97 | | 1.00 |
| Ib | 7.95 | 9.25 | | 0.24 |
| Ic | 8.20 | 9.41 | 9.69[c] | 0.07 |
| Id | 7.88 | 9.07 | | 0.45 |
| Ie | 7.11[d] | 8.89[d] | 9.03[d]    9.92[d] | 1.45 |
| IIa | 7.10 | 9.51 | | 1.00 |
| IIb | 7.42 | 9.31 | | 0.65 |
| IIc | 7.66 | 9.42 | 9.91[c] | 0.42 |

a) Vertical energy values.

b) Relative rate was determined by the ratio of $O_2$ absorption rate of a given
enamine to that of the standard enamine, (Ia) for type-(I) enamines and
(IIa) for type-(II) enamines. Reaction condition; $[S]_0$ = 5.0 x $10^{-1}$ M,
$[CuCl_2]_0$ = 1.0 x $10^{-2}$ M, $P_{O_2}$ = 760 mmHg, in chloroform solvent at 273°K.

c) Third band ($IP_3$) mainly ascribed to oxygen lone pair orbital of morpho-
lino group.

d) See Note (8).

On the purpose of mechanistic explanation of this substituent effect, preliminary kinetic studies on the oxygenation of (Ia) were performed. In the relatively lower concentration of catalyst, $[M]_0 \leq 1.0 \times 10^{-2}$ M, the kinetic data may be accomodated by the relationships,[10)]

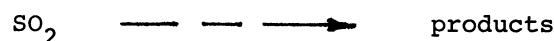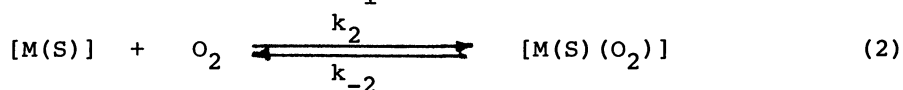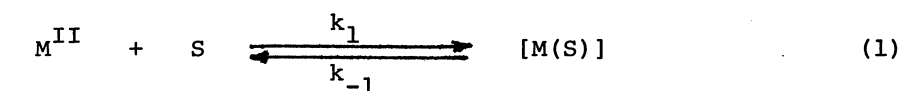$$V = -d(O_2)/dt = a[M]_0$$
$$1/V = b(1/[S]_0) + c$$
$$1/V = d(1/P_{O_2}) + e$$
$$a,b,c,d,e = const.$$

where $[M]_0$, $[S]_0$ and $P_{O_2}$ are initial cupric ion and enamine concentrations,and $O_2$ partial pressure, respectively. Same dependence was also observed on the other enamines, (Ic) and (IIb).

A possible mechanism to explain these results may be postulated as follows;



Fig. 1. Semilog plot of the relative rates of $CuCl_2$-catalyzed oxygenation of enamines vs. 1st ionization potentials.

Scheme 1.

$$M^{II} + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [M(S)] \qquad (1)$$

$$[M(S)] + O_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} [M(S)(O_2)] \qquad (2)$$

$$[M(S)(O_2)] \overset{k_3}{\longrightarrow} M^{II} + SO_2 \qquad (3)$$
$$(1,2\text{-dioxetane})$$

$$SO_2 \longrightarrow products$$

Assuming the steady state condition, the following rate equation is obtained,

$$V = \frac{k_3[M]_0[S](P_{O_2})}{K_1K_b + K_b[S] + K_a(P_{O_2}) + [S](P_{O_2})}$$

$$K_1 = k_{-1}/k_1$$
$$K_a = (k_{-2} + k_3)/k_1$$
$$K_b = (k_{-2} + k_3)/k_2$$

which satisfies the kinetic observation well.

The linear relationship between relative rates and ionization potentials strongly suggests that the rate-determining step (step 3) might involve one electron oxidation of enamine.[11)] The facility of one electron transfer reaction from enamine to cupric ion was proved by the preliminary ESR studies, which showed that the equimolar addition of enamine (Ia) to a DMF solution of $CuCl_2$ under argon atmosphere caused a large reduction (95%) in the strength of $Cu^{II}$ signals (at 0°C, after
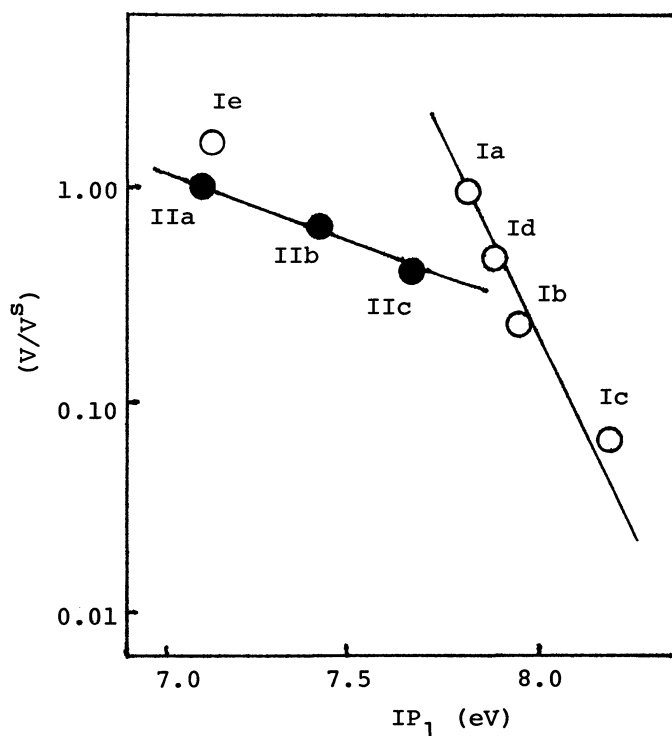
5 min). The nature of the activated form of molecular oxygen in this catalytic reaction, however, remains unclear as yet. Further mechanistic investigations are in progress.

## References and Notes

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2) (a) C. S. Foote, A. A. Dzakpasu, and J. W. -P. Lin, Tetrahedron lett., 1247 (1975). (b) H. H. Wasserman and S. Terao, ibid, 1735 (1975). (c) W. Ando, T. Saiki, and T. Migita, J. Amer. Chem. Soc., 97, 5028 (1975).

3) T. Itoh, K. Kaneda, and S. Teranishi, Tetrahedron lett., 2801 (1975).

4) In the absence of catalyst these enamines, with the exception of (IIa), did not react with $O_2$ at 0°C for 5hr. (IIa) undergoes spontaneous oxygenation even at 0°C, but the substantial rate enhancement and shortening of induction period were effected by the catalyst.

5) In a prolonged oxygenation at elevatd temperature (25∿80°), only two major products, (IV) and (V), were obtained. R. A. Jeruss, J. Org. Chem., 34. 3648 (1969).

6) The linearity of correlation between the oxidation potentials ($E_{1/2}$) and the ionization potentials (IP) has been well established. L. L. Miller, G. D. Nordblow, and E, A, Mayeda, J. Org. Chem., 37, 916 (1972).

7) The photo-electron spectra were measured with the apparatus already reported. I. Watanabe, Y. Yokoyama, and S. Ikeda, Bull. Chem. Soc. Japan., 47, 627 (1974).

8) Under these reaction conditions, the reaction rate was not influenced by the agitation speed.

9) The strong mesomeric mixing of nitrogen lone pair electrons with benzene π electrons rather than with olefinic π electrons in (Ie) remarkably lowers 1st IP level.

10) These rate expressions seem to exclude the possibility of cupric ion-initiated cation radical chain mechanism, which was previously postulated for air sensitive dienamines,[1a] because the kinetics of such chain reaction should follow the equation, $-d(O_2)/dt = k[S]^{3/2}[M]_0^{1/2}(P_{O_2})^0$, analogous to the well known metal ion-initiated oxidation of aldehyde. D. Swern, in "Organic peroxides" Vol 1. D. Swern, Ed., Wiley, New York, N. Y., 1970, p 324.

11) Similar mechanisms involving a rate-determining one electron transfer step in the ternary complex have been proposed for other oxidation reactions catalyzed by transition metal ions. M. M. T. Khan and A. E. Martell, J.Amer.Chem. Soc., 89, 4176 (1967).