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New cumene-oxidation systems
O_2 activator effects and radical stabilizer effects

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Abstract

For the purpose of increasing the efficiency of cumene hydroperoxide (CHP) production, two approaches, (A) increasing CHP generation rate by the acceleration of rate-determining step vis-à-vis CHP formation using O_2 activators, and (B) increasing CHP selectivity by the mitigation of side reactions, were carried out. As for O_2 activators, we found that a new Cu(II) complex having a pyridine–imine chelate ligand (TRIP) increased CHP formation rate with no practical decrease in CHP selectivity. Thus, TRIP displayed higher CHP formation rate and selectivity than those for conventional auto-oxidation at 90°C. Regarding the mitigation of side reactions, we focused on the reaction of CHP with a cumyl radical, resulting in a by-product formation. For suppressing this reaction, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was investigated as a radical stabilizer. As a result, TEMPO provided higher CHP selectivity compared to that of auto-oxidation at the same CHP formation rate. Therefore, two methods for increasing the efficiency of CHP production have been demonstrated.

Keywords: Oxidation; Cumene; CHP; Radical; Copper; TEMPO

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1. Introduction

Phenol and its derivatives such as alkyl phenols, bis-phenols, and catechol are important raw materials for phenol resins, polycarbonates, polyphenylene ethers, perfumes, medicines, agricultural chemicals, and so on. Industrial phenol-production process generally involves the following three steps (Scheme 1) [1]:

1. Isopropylation of benzene to cumene.
2. Auto-oxidation of cumene to cumene hydroperoxide (CHP).
3. Acid cleavage of CHP to phenol and acetone.

Among these three steps, the cumene auto-oxidation step affords the lowest efficiency [2]. Therefore, in order to enhance the efficiency of phenol production, and improving the cumene auto-oxidation step, namely increasing both CHP formation rate and CHP selectivity, is most effective. However, in cumene auto-oxidation, CHP formation rate and CHP selectivity are in a trade-off relationship because cumene auto-oxidation is subject to the decomposition of CHP.

We firmly believe that there should be a way to overcome the aforementioned trade-off relationship. Therefore, two approaches — Strategy [A] which increases CHP formation rate without decreasing CHP selectivity and Strategy [B] which increases CHP selectivity without decreasing CHP formation rate — were mapped out in an attempt to improve the cumene auto-oxidation step, namely to increase the efficiency of CHP production (Scheme 2).

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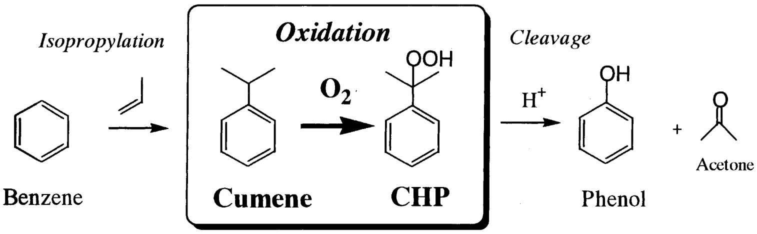


Scheme 1. Phenol-production process (cumene-oxidation method).

2. Experimental

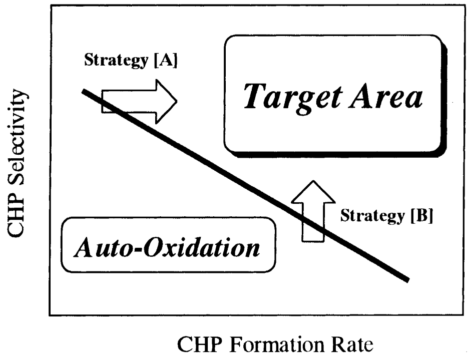
2.1. General

Materials. Starting CHP in cumene solution was prepared from cumene (Wako Pure Chemical Industries) and CHP (80% CHP in cumene solution: NOF). Salene-Co, TPP-Co, Co(II)$SO_4{\cdot}7H_2O$, $CuSO_4{\cdot}5H_2O$, 1,4,8,11-tetraazacyclotetradecane (cyclam), 2,6-pyridinedicarboxyaldehyde, *N*,*N*′-bis(3-aminopropyl)ethylenediamine-2-aminopyridine, and 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) were purchased from Wako Pure Chemical Industries, Tokyo Kasei Kogyo or Aldrich Chemical, and used without further purification.

Analysis. CHP concentration was measured by an automatic titrator for potential difference (Kyoto-Denshi). Amounts of by-products (α,α-dimethylbenzylalchohol, acetophenone, and dicumylperoxide) were determined by GC analysis. CHP formation rate and CHP selectivity were calculated using the following equations:

$$\text{CHP formation rate [wt.\%/h]} = \frac{\text{Final CHP [wt.\%]} - \text{Initial CHP [wt.\%]}}{\text{Reaction time [h]}}$$

$$\text{CHP selectivity [mol\%]} = \frac{\text{Final CHP [mol\%]} - \text{Initial CHP [mol\%]}}{(\text{Final CHP [mol\%]} - \text{Initial CHP [mol\%]}) + (\text{Final by-products [mol\%]} - \text{Initial by-products [mol\%]})}$$



Scheme 2.

2.2. Complex synthesis

Cyclam-Co(II)SO_4. A reaction of Co(II)$SO_4{\cdot}7H_2O$ with a small excess amount of cyclam in methanol at 60°C furnished cyclam-Co(II)SO_4 in 87% yield as a blue powder.

Cyclam-Cu(II)SO_4. A reaction of Cu(II)$SO_4{\cdot}5H_2O$ with a small excess amount of cyclam in methanol at 60°C furnished cyclam-Cu(II)SO_4 in 85% yield as a violet crystal.

PYC-Cu(II)SO_4. Schiff base condensation between 2,6-pyridinedicarboxyaldehyde and *N*,*N*′-bis(3-aminopropyl)ethylenediamine in ethanol to afford the corresponding cyclic pyridine–imine ligand (PYC) in

60% yield. A reaction of Cu(II)$SO_4 \cdot 5H_2O$ with a small excess amount of PYC in methanol at 60°C furnished PYC-Cu(II)SO_4 in 61% yield as a black powder.

TRIP-Cu(II)SO$_4$. A reaction of Cu(II)$SO_4 \cdot 5H_2O$ with 1 equiv. of 2,6-pyridinedicarboxyaldehyde and 2 equiv. of 2-aminopyridine in ethanol at 50°C furnished TRIP-Cu(II)SO_4 in 80% yield as a bluish-white powder.

Transition metal complexes that we prepared were given appropriate data for elemental analysis.

2.3. Cumene-oxidation

Typical cumene-oxidation procedures are described below:

1. *Preliminary screening of transition metal complexes for cumene-oxidation*. Cumene-oxidation was carried out under 0.1 MPa atmospheric pressure in a 500 ml glass reactor equipped with a propeller-like stirrer. Hundred grams of CHP/cumene solution (CHP concentration: 20 wt.%), transition metal complex (20 ppm vs cumene), and 50 g of 0.05% Na_2CO_3 aq. as a pH moderator were introduced into a reactor under nitrogen atmosphere. The mixture was thermostated to 90°C with stirring (1000 rpm), and the air feed (120 ml/min) started. After the prescribed time, an aliquot (5 ml) was removed from the reaction mixture and analyzed for amounts of CHP and by-products.
2. *Cumene-oxidation under pressurized conditions*. Cumene-oxidation was carried out under 0.7 MPa air pressure in a 1000 ml stainless steel reactor equipped with a turbine-like stirrer. Hundred and eighty grams of CHP/cumene solution (CHP concentration: ca. 22 wt.%), a catalyst, and 90 g of 0.05% Na_2CO_3 aq. as a pH moderator were introduced into a reactor under nitrogen atmosphere. The mixture was thermostated to a prescribed temperature with stirring (750 rpm), and the air feed (180 ml/min) started. After being pressurized to 0.7 MPa, an aliquot (5 ml) was removed from the reaction mixture at 30 min intervals, and analyzed for amounts of CHP and by-products. The point that CHP concentration reached at 25 wt.% was regarded as an initial point of oxidation. When CHP concentration reached 35 wt.%, the air feed was ceased to terminate the oxidation.

2.4. Theoretical calculations

The semi-empirical MO calculations were carried with the PM3 Hamiltonian using MOPAC (Ver. 6) program [3,4].

3. Results and discussion

3.1. Concepts for increasing CHP productivity

To make concepts for increasing CHP productivity, mechanism for cumene auto-oxidation was confirmed (Fig. 1). Firstly, a cumylhydroxy radical and OH radical are generated, as an initiation, by thermal decomposition of CHP. The initial step of the chain reaction is an abstraction of a benzylic hydrogen by the cumylhydroxy radical or OH radical to generate a cumyl radical and α,α-dimethylbenzylalchohol (by-product $(\mathcal{A})$) or water. Subsequently, molecular oxygen reacts with the cumyl radical to give a cumylhydroperoxy radical, this reaction being a rate-determinating step. The cumylhydroperoxy radical takes a benzylic hydrogen of another cumene to generate a CHP, the desired product, and a cumyl radical. In cumene auto-oxidation, in addition to $(\mathcal{A})$, other organic compounds such as acetophenone and dicumylperoxide were also produced as by-products $(\mathcal{B})$ and $(\mathcal{C})$, however, $(\mathcal{A})$ is the predominant by-product (Table 1). The by-product $(\mathcal{A})$ and cumylhydroxy radical, being transformed to by-product $(\mathcal{A})$, are thought to be generated mainly through thermal decomposition of CHP (Eq. (1)), the reaction between CHP and a cumyl radical (Eq. (2)), and thermal decomposition of DCP (Eq. (3)), as shown in Fig. 1. Thus, depressing the thermal decomposition of CHP (Eq. (1)) is effective for increasing CHP selectivity.

However, for depressing the thermal decomposition of CHP (Eq. (1)), lower reaction temperature, resulting in a decrease in CHP formation rate, is required. Thus, compounds capable of activating molecular oxygen were investigated. At this point, we believed that acceleration of the rate-determinating step, namely reaction between molecular oxygen and cumyl radical is a viable approach for increasing both CHP formation rate and CHP selectivity.

Alternatively, as for the side reactions (Eqs. (2) and (3)), a cumyl radical is responsible for generat-

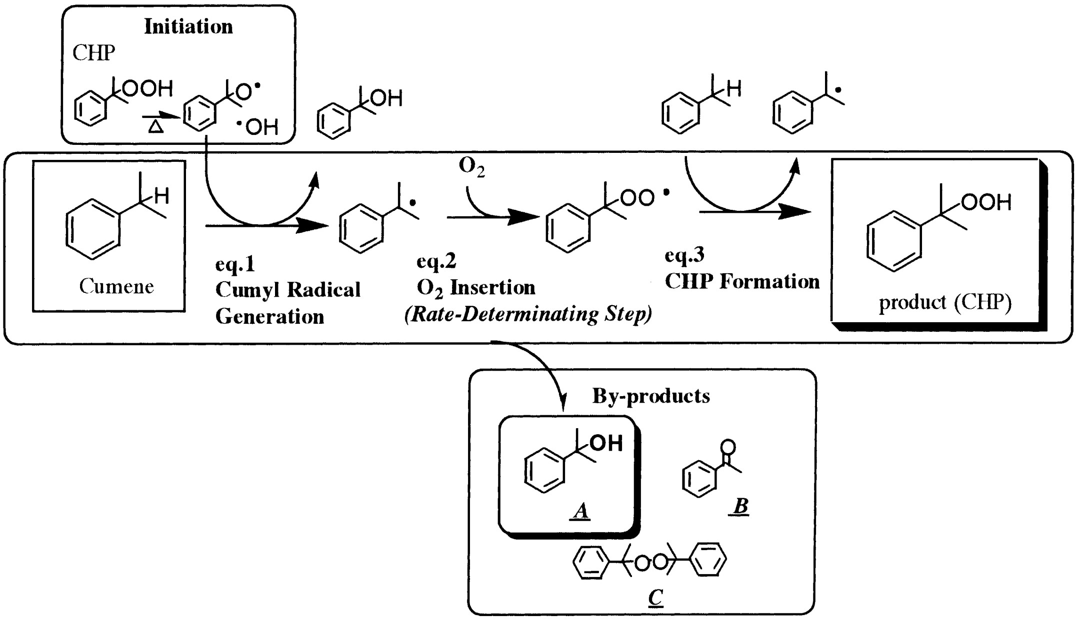


Fig. 1. Auto-oxidation mechanism.

ing by-product (*A*). Theoretical calculations suggest that the possibility of a reaction between a CHP and a cumyl radical, leading to the formation of by-product (*A*) and cumylhydroxy radical ($\Delta G = 18.2\,\text{kcal/mol}$) is at the same level as a reaction between O_2 and a cumyl radical, rate-determinating step ($\Delta G = 19.2\,\text{kcal/mol}$). Hence, we investigated radical-stabilizing reagents as an additive for cumene-oxidation to decrease the reactivity of the cumyl radical towards CHP while retaining the reactivity of it with molecular oxygen. Thus, two approaches, employment of (1) O_2 activators (for Strategy [A]), and (2) radical stabilizing reagent (for Strategy [B]), were performed to increase the efficiency of CHP production (Fig. 2).

3.2. Oxygen activator effects

Oxygen activator effects on cumene-oxidation were examined aiming at increasing the CHP formation rate without decreasing CHP selectivity (Strategy [A]). Late transition metal complexes, e.g., Co or Cu complexes are well known as a molecular oxygen activator [5–14]. Mutual interactions between the transition metal of a complex and a molecular oxygen generate various kinds of activated oxygen species, which are capable of reacting with various organic materials. However, transition metal complexes with highly activating molecular oxygen often decompose a product or an intermediate compound, resulting in low reaction efficiency. Thus,

Table 1
Conventional auto-oxidation results (105°C)[a]

	Initial (mmol)	Final (mmol)	Increased (mmol)	Selectivity (mol%)
CHP	300.6	406.5	105.9	86.4
By-product (*A*)	26.3	40.5	14.2	11.6
By-product (*B*)	3.4	5.6	2.2	1.8
By-product (*C*)	0.9	1.2	0.3	0.2

[a] Conditions: 0.7 MPa; reaction time, 2 h; air feed, 180 ml/min; CHP concentration, 25.4–34.4 wt.%.

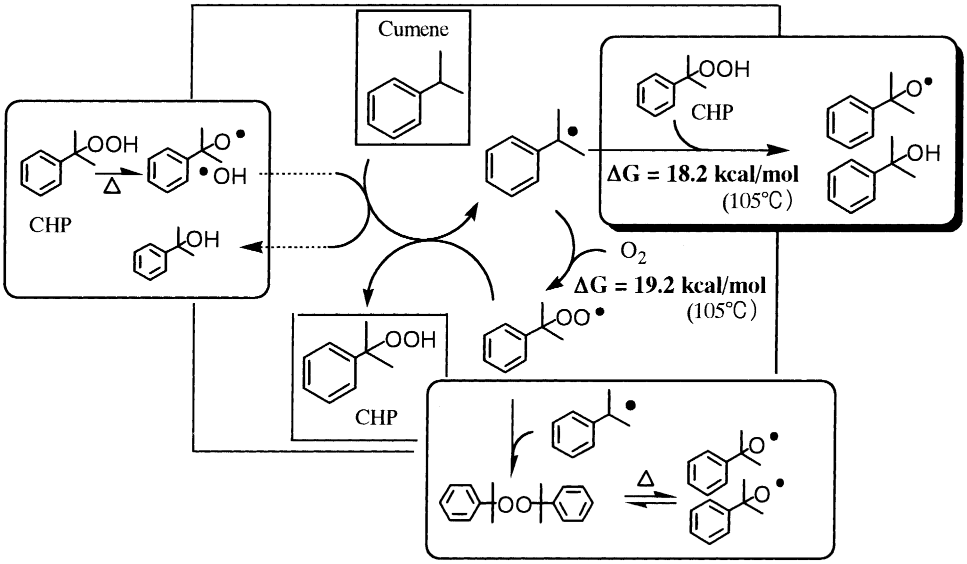
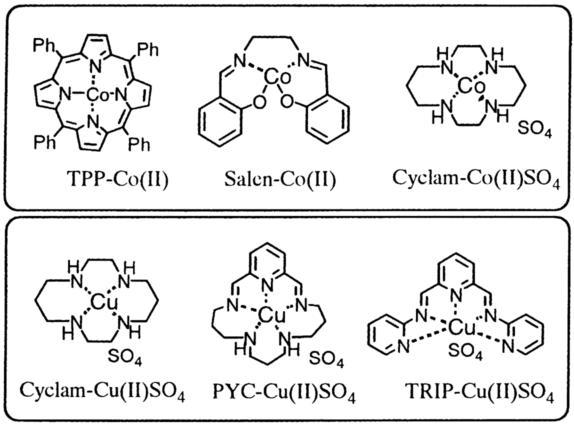


Fig. 2. Plausible by-product formation pathways (ΔG was calculated by PM3 calculation).

we focused on mild oxygen activators, which are expected to properly activate molecular oxygen to increase CHP production rate without decomposing CHP.

Preliminary screening results for cumene-oxidation at 90°C in the presence of a transition metal complex possessing 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine (TPP), *N*,*N*′-bis(salicylidene)ethylenediamine (Salen), or 1,4,8,11-tetraazacyclotetradecane (cyclam) as a ligand are summarized in Table 2. For comparison, conventional auto-oxidation for cumene was conducted under the same conditions in the absence of a transition metal complex (initial CHP concentration: 20 wt.%). As a result, CHP formation rate was 1.6 wt.%/h with a CHP selectivity of 92.4 mol% for conventional auto-oxidation. When TPP-Co(II) complex, which is a well-known oxidation catalyst in the presence of O_2, was used as an oxygen activator, both CHP formation rate and CHP selectivity were dramatically decreased. This is because TPP-Co(II) decomposes CHP probably due to its strong electron-donating properties (HOMO energy level of TPP: −0.71 eV). As Salen and cyclam have lower HOMO energy levels (Salen: −1.61 eV, cyclam: −9.13 eV) than TPP, being expected to be less electron donative than TPP, Salen-Co(II) and cyclam-Co(II)SO_4 were tested as a cumene-oxidation catalyst in the same manner.

Table 2
Preliminary screening results[a]



Catalyst	CHP formation rate (wt.%/h)	CHP selectivity (mol%)
Auto-oxidation (no catalyst)	1.6	92.4
TPP-Co(II)	0.5	51.3
Salen-Co(II)	2.6	61.6
Cyclam-Co(II)SO_4	3.1	76.8
Cyclam-Cu(II)SO_4	2.7	90.4
PYC-Cu(II)SO_4	3.0	90.8
TRIP-Cu(II)SO_4	3.7	91.1

[a] Conditions: 90°C; 0.1 MPa; initial CHP concentration, 20 wt.%; air feed, 120 ml/min; reaction time, 3 h; cat., 20 ppm.

Finally, Salen-Co(II) displayed higher CHP selectivity (61.6 mol%, CHP formation rate: 2.6 wt.%/h) than that displayed by TPP-Co(II). Moreover, using cyclam-CoSO$_4$ as a catalyst, CHP selectivity was further increased to 76.8 mol% at a CHP formation rate of 3.1 wt.%/h.

Alternatively, changing the central metal from Co(II) to Cu(II), oxidation performance was improved. Cyclam-Cu(II)SO$_4$ displayed 2.7 wt.%/h of CHP formation rate with 90.4 mol% of CHP selectivity. These results may suggest that the electron donation ability of cyclam-Cu(II)SO$_4$ is lower than that of cyclam-Co(II)SO$_4$, and thus, cyclam-Cu(II)SO$_4$ displays lower reactivity towards CHP having high electron acceptance ability.

With these results in mind, further research on other copper complexes having a neutral polyamine ligand was performed. As a consequence, we found that neutral polyamine ligands having a pyridine–imine moiety further enhanced cumene-oxidation performance without decreasing CHP selectivity. Thus, PYC-Cu(II)SO$_4$ and TRIP-Cu(II)SO$_4$ displayed 3.0 and 3.7 wt.%/h of CHP formation rates with 90.8 and 91.1 mol% of CHP selectivities, respectively.

TRIP-Cu(II)SO$_4$ was tested under pressurized (0.7 MPa) atmosphere. The oxidation performance of TRIP-Cu(II)SO$_4$ exceeded that of conventional auto-oxidation at the same CHP formation rate, as shown in Fig. 3, because of the decrease in CHP decomposition due to the lower oxidation temperature.

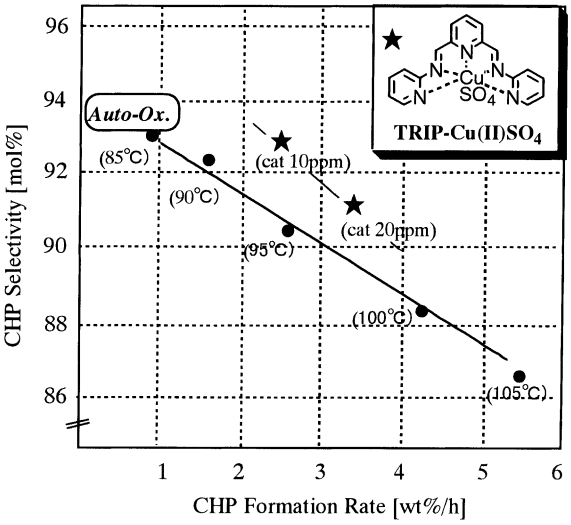
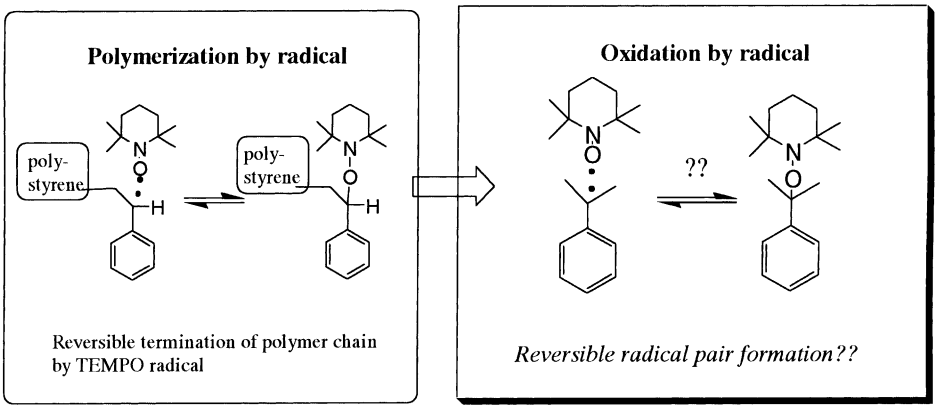


Fig. 3. Oxidation performance of TRIP-Cu(II)SO$_4$ (conditions: 90°C; 0.7 MPa; CHP concentration, 25–35 wt.%, air feed, 180 ml/min).

3.3. Radical stabilizer effects

For increasing CHP selectivity without decreasing CHP formation rate (Strategy [B]), suppressing side reactions in cumene-oxidation is effective. In this study, we focused on the reaction of CHP with a cumyl radical as a target side reaction. In order to inhibit the reaction of CHP with the cumyl radical, depressing the reactivity of the cumyl radical towards CHP, namely stabilizing the cumyl radical,



Scheme 3.

was thought to be effective. However, too much stabilization of the cumyl radical results in a termination of the chain reaction for the auto-oxidation. Thus, we must properly stabilize the cumyl radical, as not to react with CHP but with molecular oxygen, leading to the decrease in the side reaction without terminating CHP formation. In other words, appropriate stabilization of the cumyl radical is a must for increasing CHP selectivity without decreasing CHP formation rate.

In the field of radical polymerization, quite a few researchers have postulated the idea of using the reversible termination of the growing polymer chain in a radical polymerization to give a pseudo-living polymer that is capable of stepwise chain growth [15–20], as shown in Scheme 3. This chemistry relies extremely on the selective ability of nitroxyl radicals to trap carbon-centered radicals and the apparent reversible nature of the C–O bond. We applied this concept to the cumene-oxidation system to establish a reversible radical pair formation of a cumyl radical with a nitroxyl radical.

Three kinds of radical species, a cumyl radical, a cumylhydroxy radical, and a cumylhydroperoxy radical, are mainly involved in the reaction (Fig. 1). Theoretical calculations suggest that TEMPO, a nitroxyl radical, interacts most strongly with a cumyl radical among the three radical species mentioned above (Fig. 4). This indicates that we can expect a reversible radical pair formation between a cumyl radical and a TEMPO. Consequently, we tested 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as a radical stabilizer for cumene-oxidation.

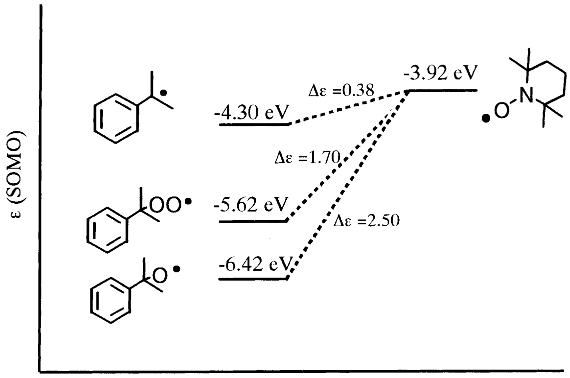


Fig. 4. Reactivity of radicals with TEMPO.

In the presence of TEMPO (200 ppm), cumene-oxidation was performed at 95°C. As a result, this oxidation system was revealed to display 93.0 mol% of CHP selectivity with 2.0 wt.%/h of CHP formation rate. This CHP selectivity was higher than that of auto-oxidation (91.5 mol%, estimated by intrapola-

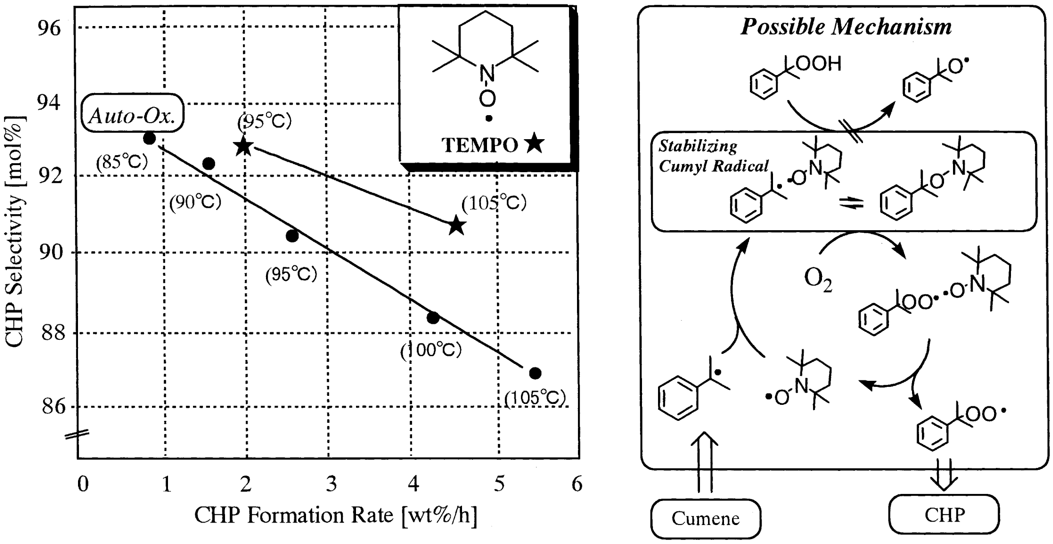


Fig. 5. TEMPO effect for cumene-oxidation (conditions: 0.7 MPa; CHP concentration, 25–35 wt.%; air feed, 180 ml/min).

tion) at the same CHP formation rate (2.0 wt.%/h) as shown in Fig. 5. By increasing the oxidation temperature from 95 to 105°C, the TEMPO system showed enhanced CHP formation rate with higher CHP selectivity than auto-oxidation at the same CHP formation rate. Thus, at 105°C, the system displayed a CHP selectivity of 91.0 mol% with CHP formation rate of 4.6 wt.%/h (auto-oxidation; 88.1 mol% CHP selectivity, estimated by intrapolation). Therefore, another new system exhibiting higher cumene-oxidation performance than the auto-oxidation has been established. In addition to TEMPO, other radical stabilizers may have potential for increasing CHP production efficiency.

4. Conclusion

In conclusion, two new methods for increasing the efficiency of CHP production have been established. Thus, copper complexes possessing neutral polyamine ligands are shown to be effective for enhancing CHP production efficiency, in particular, TRIP-Cu(II)SO_4 displays very high oxidation performance exceeding that for conventional auto-oxidation. Moreover, a radical stabilizer, TEMPO is demonstrated to realize high cumene-oxidation performance, also exceeding that for conventional oxidation. In future, we believe that both of these methods will lead to innovation for (cumene) auto-oxidation technology.

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