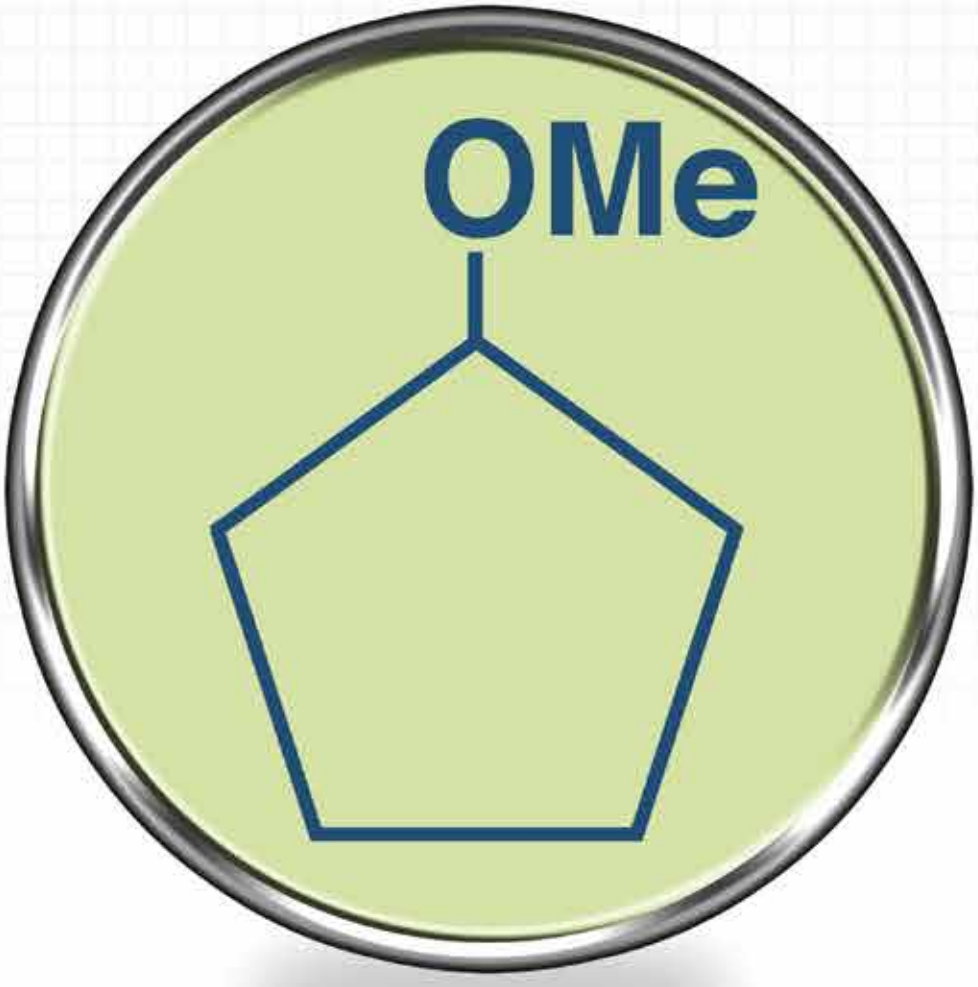
Novel hydrophobic ether solvent

Cyclopentyl methyl ether

CPME

Technical Data



ZEON CORPORATION

CONTENTS

1 Benefits of CPME

HIGH HYDROPHOBICITY

Easy separation and recovery from water, reducing emissions and wastewater
Wide applicability as a reaction, extraction and crystallization solvent, giving simple and One-pot syntheses

WIDE LIQUIDITY RANGE

Wide applications from lower to higher temperature, accelerating reaction rate

LOW HEAT OF VAPORIZATION

Saving energy for distillation and recovery

RESIST PEROXIDE FORMATION

Low exothermic decomposition energy of solvent containing it's peroxides

NARROW EXPLOSION AREA

STABLE TO ACIDS OR BASES

EASY DRYING

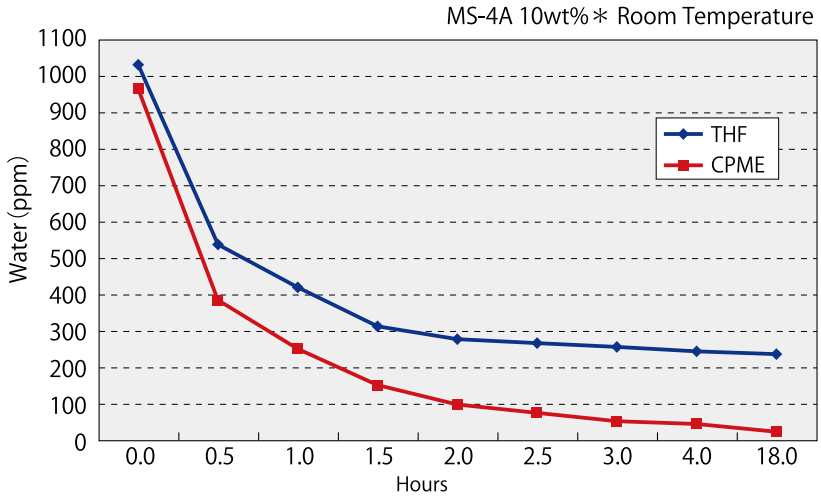
2 Physical Properties

	CPME	MeTHF	THF	Diethyl ether	Dioxane	MTBE
Relative density	0.86	0.85 *d	0.89 *a	0.71 *b	1.03 *a	0.70 *a
Vapor specific gravity (air=1)	3.45	2.97 *d	2.5 *a	2.6 *a	3.0 *a	3.0 *a
Boiling point [℃]	106	80.2 *d	66 *a	35 *a	101 *a	55 *a
Melting point [℃]	<-140	-136 *d	-108.5 *a	-116 *a	12 *a	-109 *a
Viscosity (20℃) [cP]	0.57	0.46 (25℃) *d	0.55 *b	0.24 *b	1.31 *b	
Surface tension (20℃) [mN/m]	25.17		26.4 *b	17.3 *b	36.9 *b	
Heat of vaporization (boiling point) [kcal/kg]	69.2	87.1 *d	98.1 *b	86.1 *b	98.6 *b	
Specific heat (20℃) [kcal/kg・k]	0.435		0.469 *b	0.584 *c	0.41 *b	
Dielectric constant (25℃)	4.76	6.97 *d	7.58 *b	4.20 *b	2.24 *b	
Azeotropic temperature with water [℃]	83	71 *d	64 *c	34 *b	88 *b	
Azeotropic composition (Solvent / Water, wt%)	83.7/16.3	89.4/10.6 *d	94.0/6.0 *c	98.7/1.3 *b	81.6/18.4 *b	
Solubility in water (23℃) [g/100g]	1.1	14 (20℃) *d	∞ *a	6.9 (20℃) *a	∞ *a	4.2 *a
Solubility of water in solvent (23℃) [g/100g]	0.3	4 (20℃) *d	∞ *b	1.2 *b	∞ *b	
Flash point [℃]	-1	-11 *d	-14.5 *a	-45 *a	12 *a	-28 *a
Auto Ignition temperature [℃]	180	270 *e	321 *a	160-180 *a	180 *a	375 *a
Explosion range [vol%] Lower limit	1.1	1.5 *e	2 *a	1.7 *a	2 *a	1.6 *a
Upper limit	9.9	8.9 *e	11.8 *a	48 *a	22 *a	15.1 *a

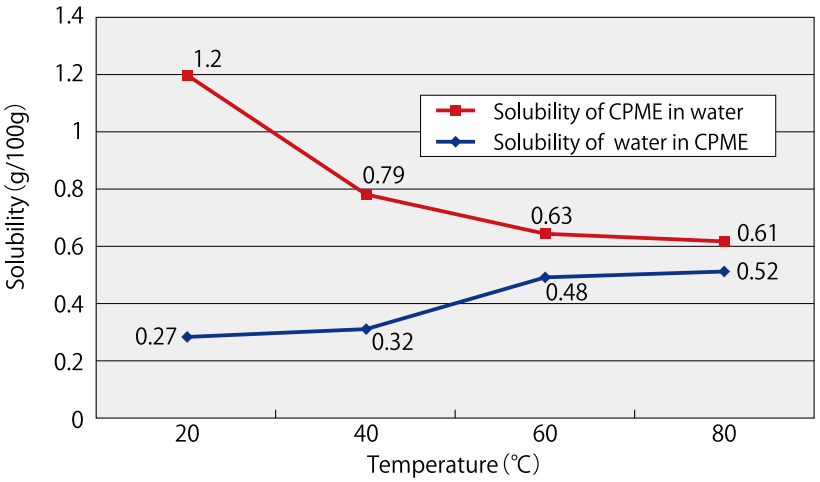
ref ;
*a ; International Chemical Safety Cards (ICSC)
*b ; 溶剤ハンドブック、講談社 (1989) (Youzai hand book, Kodansha Ltd. , 1989)
*c ; 溶剤ポケットブック、オーム社 (2001) (Youzai pocket book, Ohmsha,Ltd. , 2001)
*d ; Org. Process Res. Dev.,2007, 11 (1), pp 156-159
*e; Penn A Kem, Methyltetrahydrofuran, MSDS Date: 10/1/2010

3 High Hydrophobicity

(1) Drying by Molecular sieves

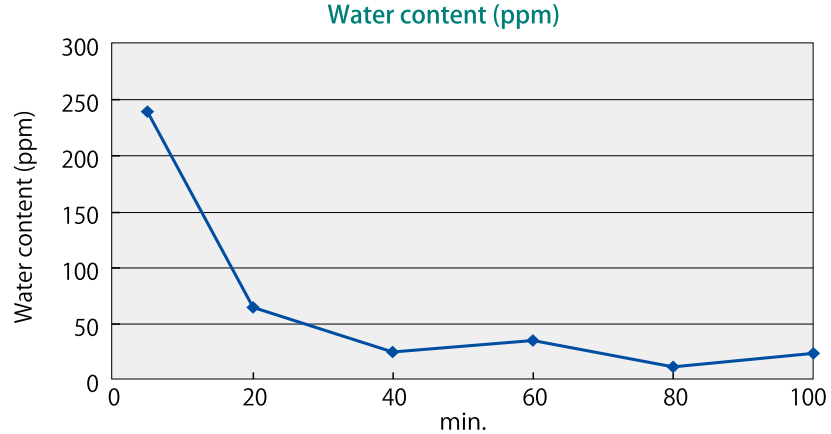


(2) Solubility of CPME vs. Water



(3) Azeotropic distillation of CPME with Dean-Stark Trap

Conditions : CPME saturated with water was refluxed with Dean-Stark Trap and then water content was monitored.



(4) Distillation of CPME saturated with water

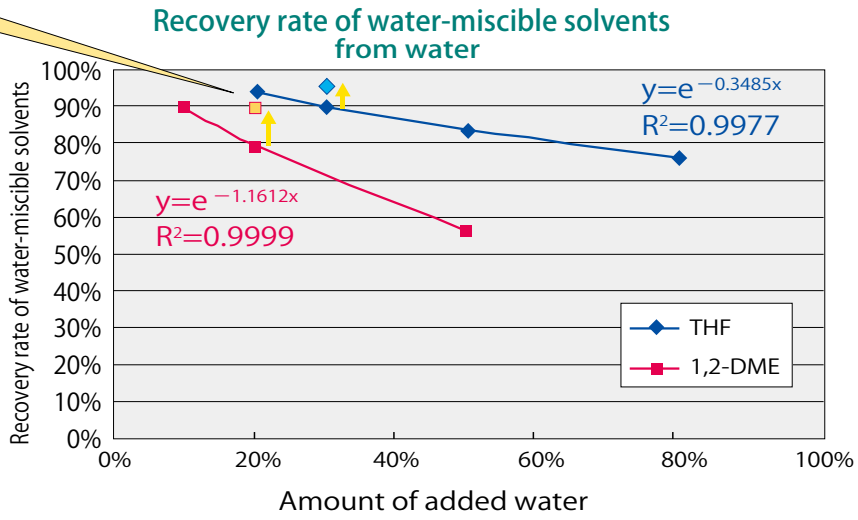
Fractional Distillation of CPME saturated with water (500g)

Fraction	Boiling Point (℃)	Weigjt (gram)	CPME (%)	Water (ppm)
1	81-84	11	99.3	
2	84-105	10	99.9	617
3	105-106	454	99.9	92
Residue		24		
Total		498		

(5) Recovery of water-miscible solvents from water

Conditions : At room temperature, equal weight of CPME and water-miscible solvents (THF and 1,2-Dimethoxyethane) were mixed. Water was added, shaken for 10 minutes and left for 1 minute.

Recovery rate can be improved with saturated aq. NaCl



Recovery rate of CPME is higher than 95% because of its Hydrophobicity.

(6) Azeotropes with other solvents

Solvents with which CPME forms azeotropes

Solvent	Boiling Point of Solvent (℃)	Azeotropic temperature (℃)	Composition Solvent / CPME (wt%)
Water	100	83	16/84
Methanol	65	63	85/15
Dimethyl carbonate	90	90	67/33
Acetonitrile	82	82	63/37

Solvents with which CPME does not form azeotropes

Ketones	Acetone MEK MIBK
Hydrocarbons	n-Hexane n-Heptane* Toluene*
Ethers	THF DME
Alcohols	IPA
Esters	Ethyl acetate
Others	DMSO

* Hard to separate

(7) Azeotropes with water at different pressures

Pressure (kPa)	Azeotropic Temperature (℃)	Composition Water/CPME (wt%)
101.3	83.0	16.3/83.7
19.1	44.7	19.6/80.4
11.4	34.2	19.5/80.5
7.5	26.1	17.5/82.5

(8) Distribution of ketones between CPME and water

Conditions : Ketones were added to mixture of 10g of CPME and 5g of ion-exchange water. The mixtures were cooled down to 5℃ and vigorously shaken. They were cooled down to 5℃ again.

Acetone

Amount of Acetone	Weight ratio of Acetone	
	Layer of CPME	Layer of Water
1g	0.49	0.51
2g	0.53	0.47
4g	0.58	0.42

MEK

Amount of MEK	Weight ratio of MEK	
	Layer of CPME	Layer of Water
1g	0.83	0.17
2g	0.85	0.15
4g	0.88	0.12

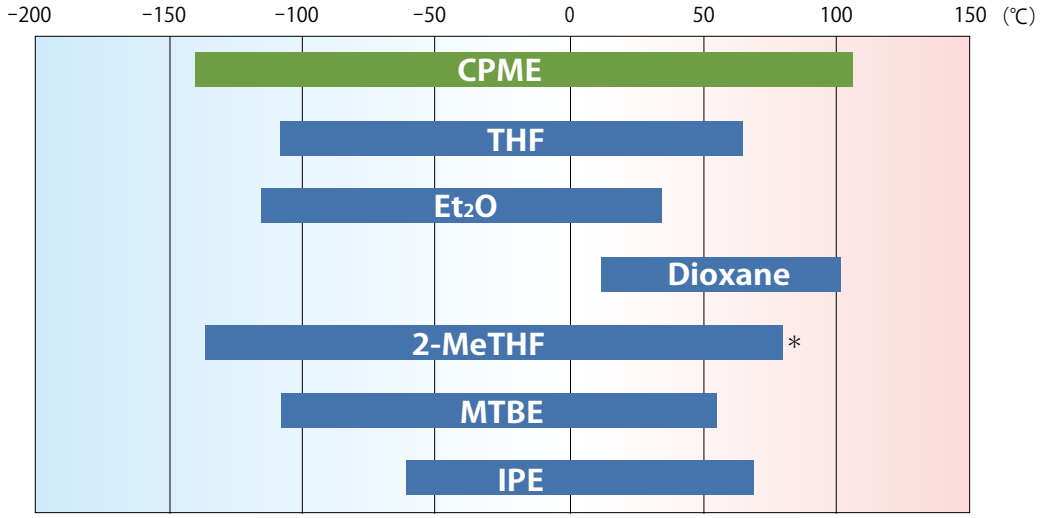
MIBK

Amount of MIBK	Weight ratio of MIBK	
	Layer of CPME	Layer of Water
1g	0.99	0.01
2g	0.99	0.01
4g	0.99	0.01

The solubility of CPME in water was around 1%.

4 Wide Liquidity Range

Liquidity range of ether solvents



ref. : International Chemical Safety Cards (ICSC)
＊: Org. Process Dev., 2007, 11(1), PP 156-159

5 Low Heat of Vaporization

Evaporation rate

Method : ASTM D 3539-87 Standard Test Methods for
Evaporation Rates of Volatile Liquids by Shell Thin-Film Evaporometer
Conditions : 23℃ x50%RH

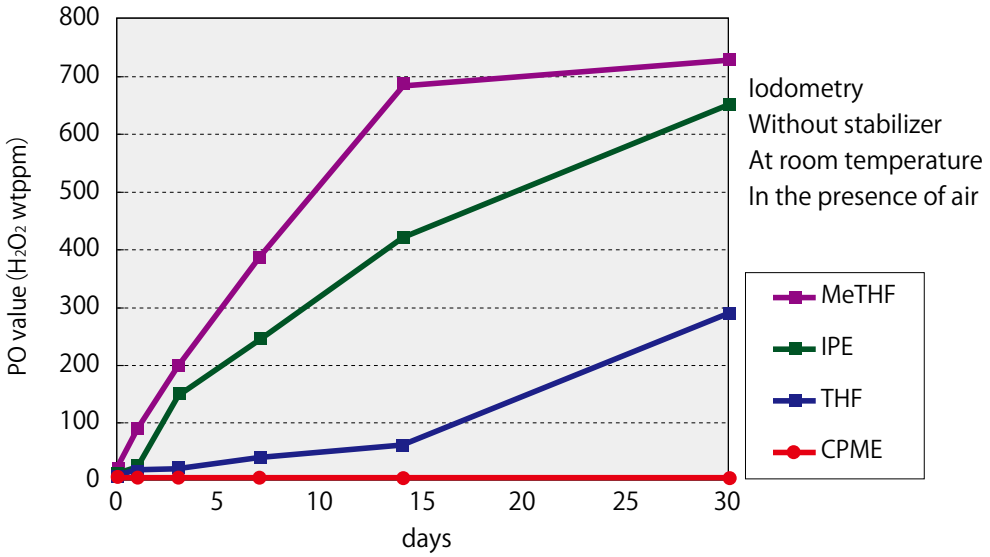
Solvent	Relative evaporation rate
CPME	3.5
Butyl acetate	1

6 Peroxide Formation

(1) Peroxide Formation of Ether Solvents

Conditions :

- 20ml of each sample in a brown bottle (capacity: 65 ml)
- CPME : Distilled over with benzophenone-sodium mixture
  THF (Tetrahydrofuran) : commercially available dried product without stabilizers (Wako)
  MTBE (Methyl t-butyl ether): commercially available dried product without stabilizers (Aldrich)
  IPE (Diisopropylether) : Distilled over with benzophenone-sodium mixture of a commercial product (Aldrich)
- Storage : at room temperature, in a dark place, in the presence of air
  Measurement times: after 0, 1, 3, 7, 14, 30 days
  Number of samples n = 2
- Titration method : Add aq.acetic acid, aq.KI and titrate produced I_2 with aq.sodium thiosulphate (lower limit: 1 ppm)



(2) SC-DSC Analysis

Conditions : Sealed cell type, in the air

Peroxide value (H_2O_2 wt ppm)	Exothermic intiation temperature (℃)	Heat Generation (J/g)
4.5	128.4	61.4
30.0	122.0	67.0
150.0	129.5	77.9

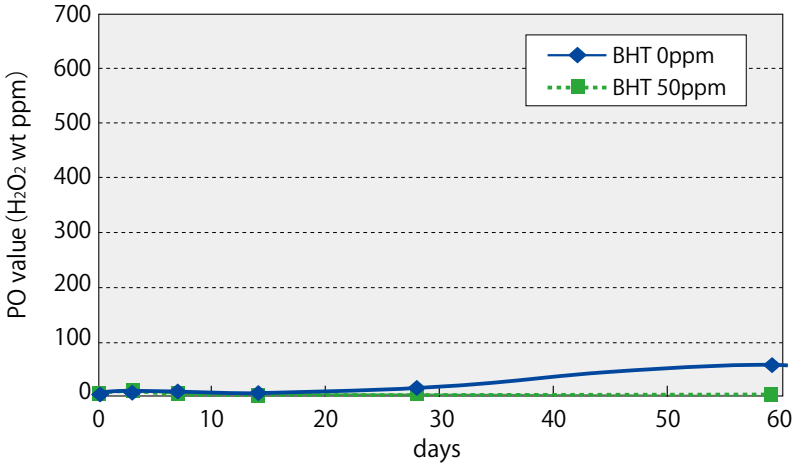
(3) ARC Test (Accelerating Rate Calorimeter)

- **Pressurization by air to 5 atm**：Temprature rise by 1.5℃ at 106℃ No heat generation afterward
- **Pressurization by nitrogen to 5 atm**：No heat generation

(4) Effect of Stabilizer to Peroxide Formation

Conditions :
at 40℃, in the presence of air, in a dark place

Peroxide & BHT content



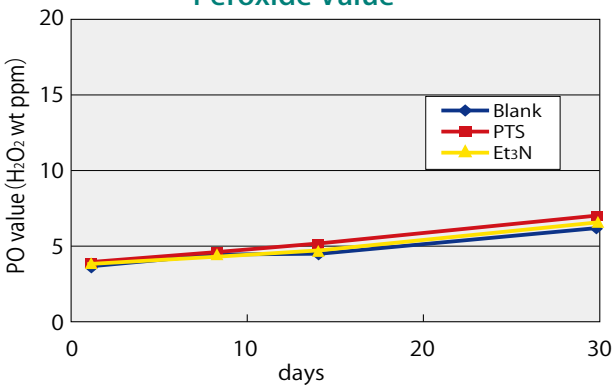
(5) Effects of Additives to Peroxide Formation

Conditions : at room temperature, in the presence of air, in a dark place

(1) Acid and Base:100ppm each

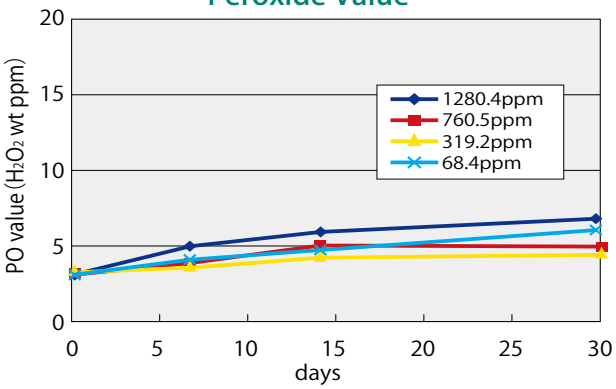
Acid：PTS=p-Toluenesulfonic acid　Base：Et_3N=Triethylamine

Peroxide Value



(2) Water

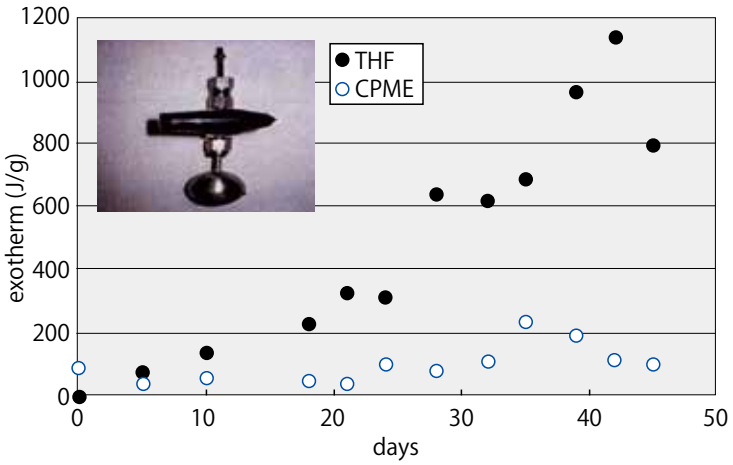
Peroxide Value



(6) Exothermic energy under O_2

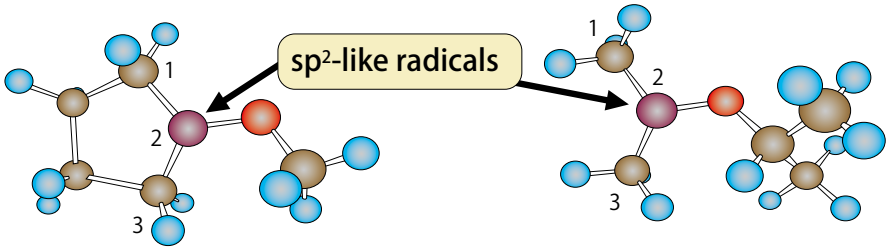
Miyake, et al., 12th International Symposium on Loss Prevention and Safety Promotion in the Process Industries

Conditions : CPME and THF without an antioxdant which were pressurized with 0.99MPa of O_2 in SUS316 closed vessel were stored at 40℃. The material was sampled at adequate interval time and the thermal analyses were carried out by using differential scanning calorimetry (DSC).



(7) MM3 simulation analysis

Kubo, H.; Sakakibara, K.; Yoshizawa, K.; Watanabe, K.; Yuzuri, T. The 85th Spring Meeting of Chemical Society of Japan (2005).



CPME radical　　IPE radical

MM3 simulation

Ether radical	CPME	IPE
Bond Angle (°)	115.6	119.9
Heat of Formation (kcal/mol)	44.2	40.9
Strain Energy (kcal/mol)	62.4	55.3

As a result of the simulation, the structural strain of CPME radical is calculated to be greater then that of IPE radical because of its five-membered ring structure. That should hardly cause formation of CPME radical itself. Therefore, the unstable radical of CPME is supposed to be the reason of low peroxides formation of CPME.

(8) Removal of Peroxide with aq. Na_2SO_3

Preparation :

CPME 1kg (Purity : 99.9% Peroxide : 5ppm)

↓ stir in the air at 80℃ for 4hr

CPME 1kg (Purity : 99.5% Peroxide : 620ppm)

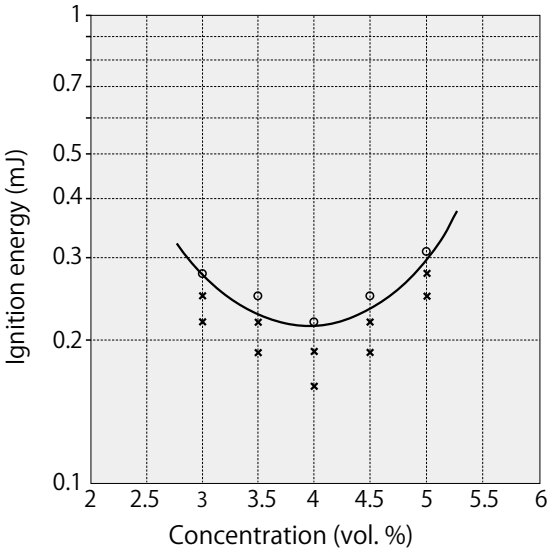
Conditions : 1kg of CPME containing peroxide washed with 500g of 5% Na_2SO_3 several times.

Number of washing (times)	Peroxide value (H_2O_2 wt ppm)
0	620
1	116
2	95
3	7.5

7 Narrow Expansion Area (Static Electricity)

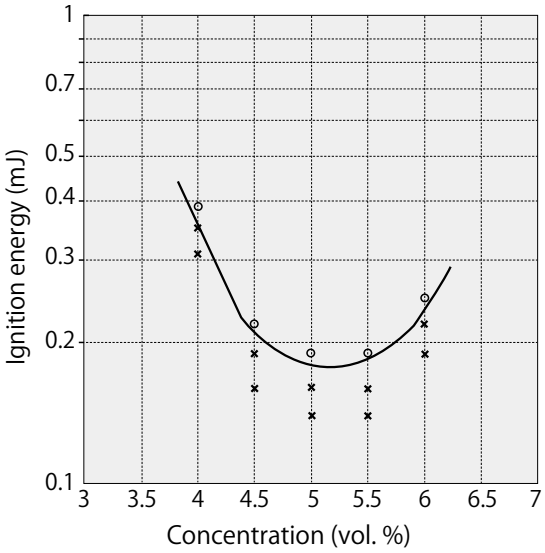
(1) Minimum ignition energy *(E)*

CPME



0.19mJ<E<0.22mJ
at about 4% concentration, 33℃

THF



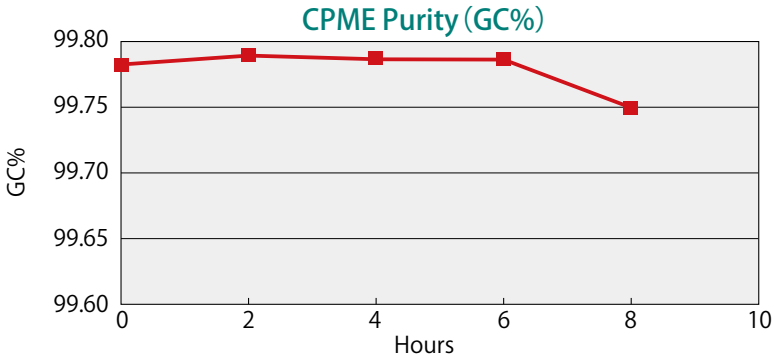
0.16mJ<E<0.19mJ
at about 5% concentration, 23℃

(2) Electrical resistivity

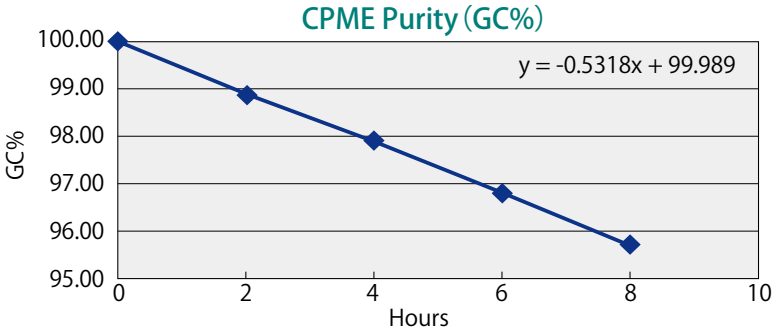
Solvent	Volume Resistivity (Ω·cm)	Temperature (℃)	Relative Humidity (%)
Cyclohexane	2.1×10^{14}	9	58
Toluene	2.5×10^{13}	27	54
Xylene	2.8×10^{13}	28	54
CS_2	7.5×10^{11}	10	57
CPME	5.0×10^{9}	20	55
AcOBu	9.2×10^{8}	27.7	54
AcOEt	1.7×10^{7}	27.7	54
MeOH	$<4.0\times10^{6}$	27.7	54
EtOH	$<4.0\times10^{6}$	27.7	54
BuOH	$<4.0\times10^{6}$	27.7	54
Acetone	$<4.0\times10^{6}$	27.7	54
MEK	$<4.0\times10^{6}$		-
MIBK	$<4.0\times10^{6}$	27.7	54
CCl_4	1.0×10^{14}	9.5	57

8 Stability to acids

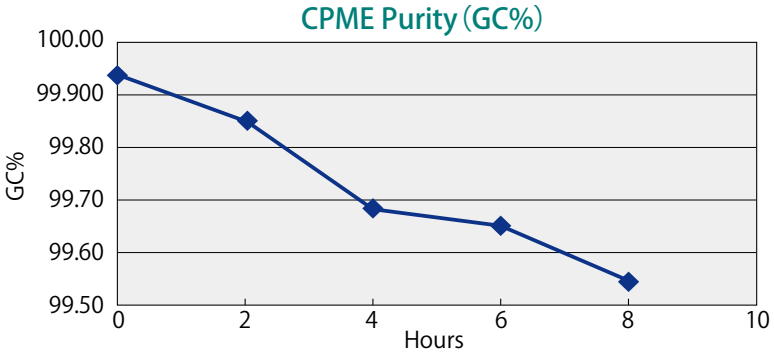
(1) 18% HCl〈Heterogeneous system〉(1/1 vol., at 40℃)



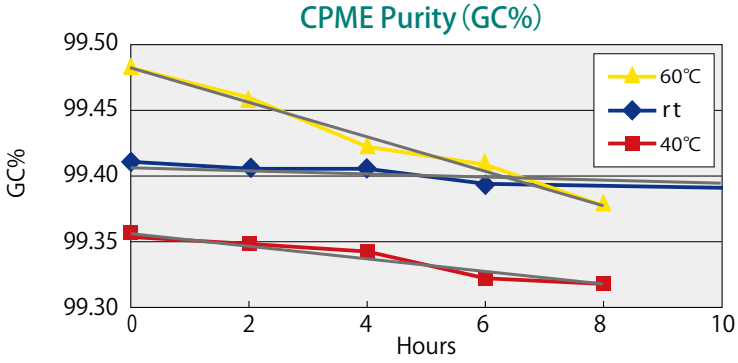
(2) 18% HCl〈Heterogeneous system〉(1/1 vol., at 100℃)



(3) 36% HCl〈Homogeneous system〉(1/1 vol., at 26℃)



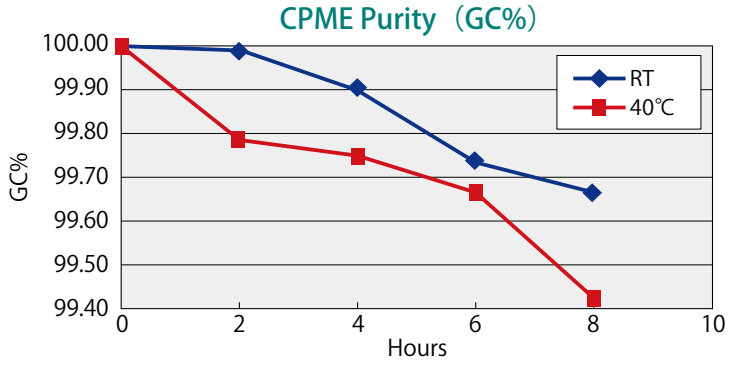
(4) 4N HCl-CPME* 〈Homogeneous system〉



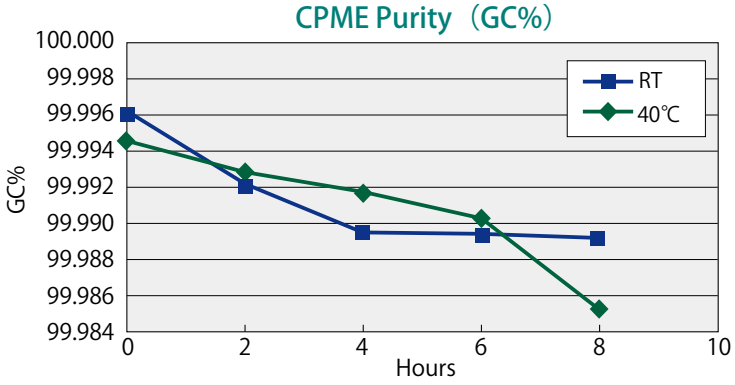
60℃: y= -0.0127x + 99.482
rt : y= -0.0012x + 99.407
40℃: y= -0.0052x + 99.358

*Product of Watanabe Chemical Industries, Ltd.

(5) 62% H_2SO_4 〈Homogeneous system〉(1/1 vol.)

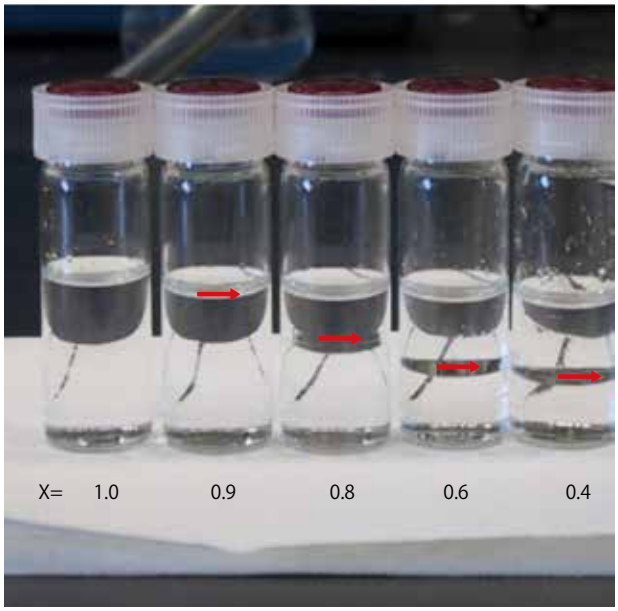


(6) conc.H_2SO_4 〈Homogeneous system〉(H_2SO_4/CPME=1/10 wt.)



(7) Compatibility of CPME with sulfuric acid

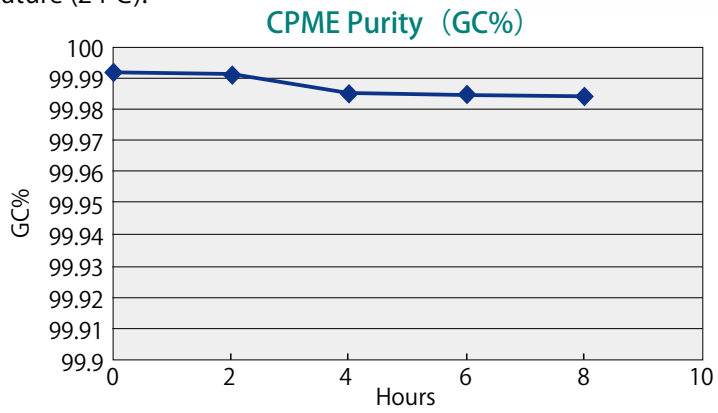
Water (ml)	conc.H_2SO_4 (ml)	H_2SO_4 (wt%)	
1	1	61.1	Compatible
1	0.9	58.7	Partially Compatible
1	0.8	56.1	Partially Compatible
1	0.6	49.3	Separate
1	0.4	39.8	Separate



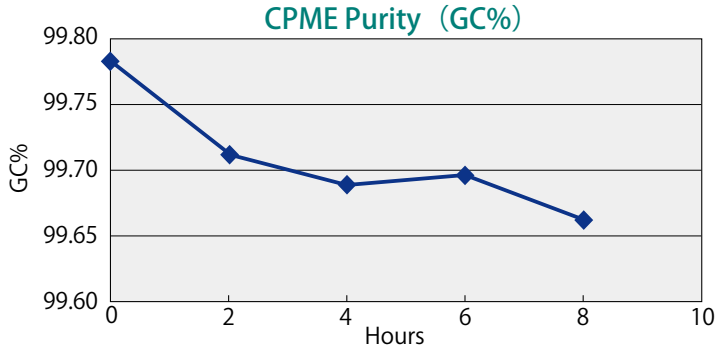
10 minutes after mixing Water:1ml＋H_2SO_4:Xml＋CPME:2ml

(8) 65% conc. HNO_3 〈Homogeneous system〉(HNO3/CPME=1/10wt., 24℃)

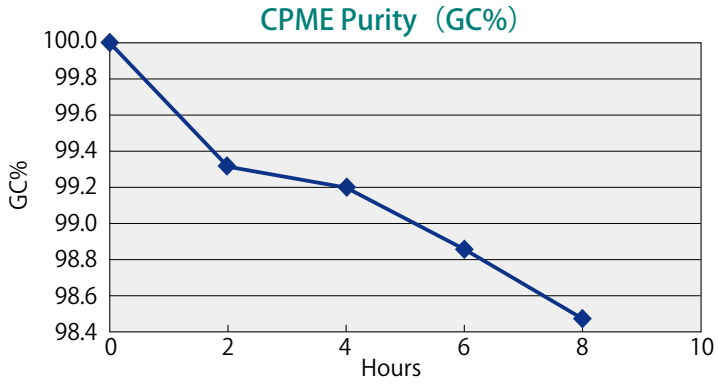
Conditions : 2g of 65% conc. HNO_3 was added slowly to 20g of CPME at 0℃, and stirred for 8 hours at room temperature (24℃).



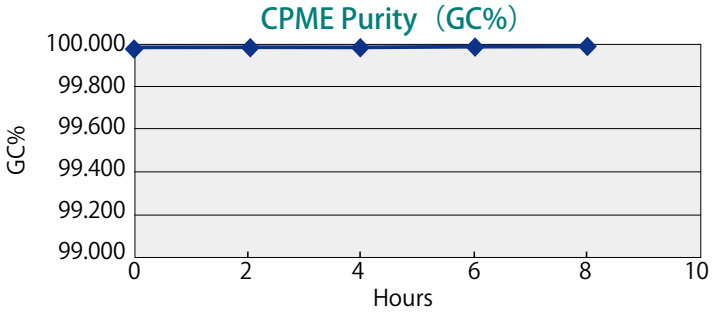
(9) 0.1M Camphor sulfuric acid 〈Homogeneous system〉(at reflux temperature)



(10) Methyl trifluoromethanesulfonate 〈Homogeneous system〉(MeOTf/CPME=1/10 wt., 25℃)



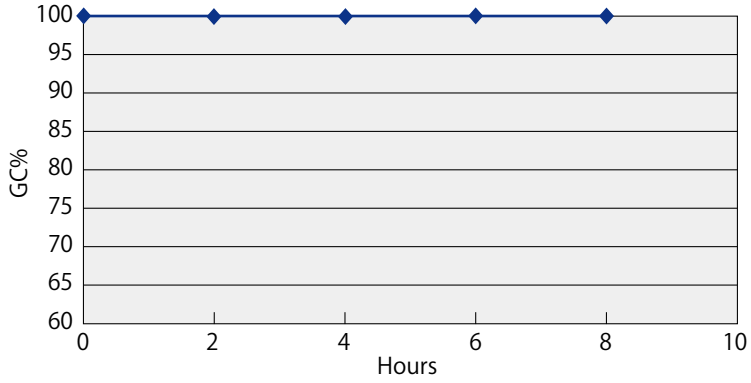
(11) Trifloroacetic acid 〈Homogeneous system〉(TFA/CPME=1/10wt., 22℃)



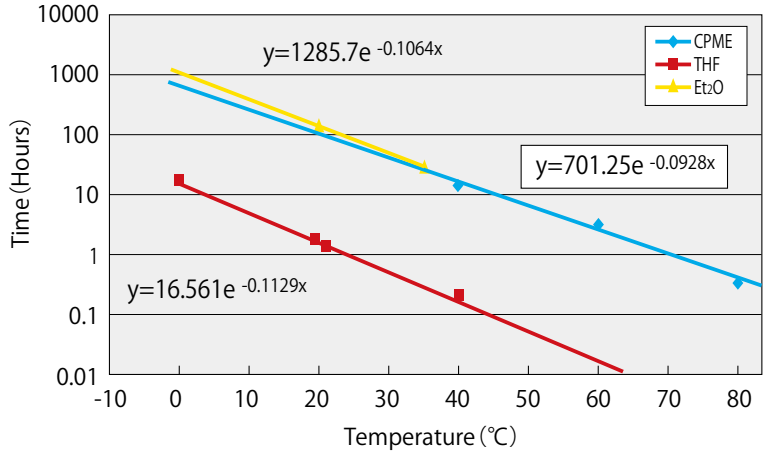
9 Stability to Bases

(1) 85% KOH 〈Heterogeneous system〉(KOH/CPME=35/100 wt., 110℃)

Conditions : 35g of 85% KOH pellets were added to 100g of CPME, and then refluxed for 8 hours under nitrogen at 110℃.



(2) Half-Lives of n-BuLi in Ethers



- 1.6M of n-BuLi in n-Hexane solution
- n-BuLi : Ethers=5ml:10ml
- Bipyridyl-Butanol titration method

10 Solubility of Gases

(1) Hydrogen solubility in solvents

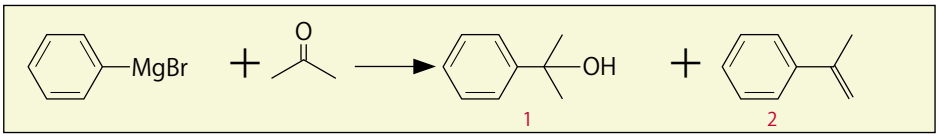
Solvent	Temperature(℃)	Solubility(ml/l)
CPME	18	110
THF	21	96
Acetone	18	99

(2) Oxygen solubility in solvents

Solvent	Temperature(℃)	Solubility(ml/l)
CPME	16	330
THF	21	390

11 Reactions

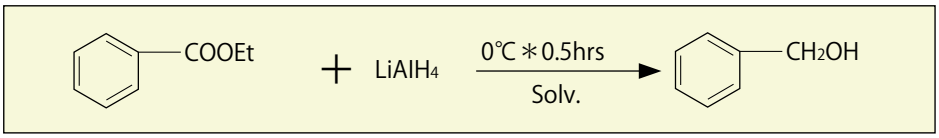
(1) Grignard Reaction



Solvent	Yield of Products(%)		Sel.of Products(%)	
	1	2	1	2
THF	44.8	33.1	57.5	42.5
THF＋CPME	66.8	14.7	82.0	18.0
CPME	81.9	1.6	98.0	2.0

Conditions : ● Grignard reagent concentration 1 mol/l
● Temperature: O℃＊1hr＋reflux＊1h
● Work-up: 1N-HCl＊rt

(2) LAH Reduction



Conditions : Substrate : LAH : Solvent=10mmol : 10mmol : 30ml
Solvents : Diethyl Ether or CPME

Work-up :

① Acid treatment Water 1ml → 10%HCl 20ml → washing with water in 2times

② Alkaline treatment Ethyl acetate 2ml → 40%NaOH 10ml → water 5ml

(yield：GC internal standard method)

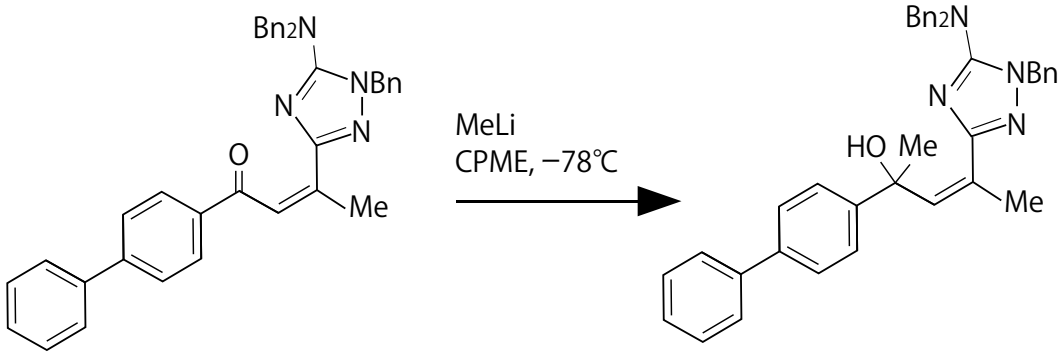
Work-up	CPME	Diethyl Ether	Remarks
①	Organic layer 83.5 Aqueous layer 6.1 Total 89.6	Organic layer 66.3 Aqueous layer 21.1 Total 87.4	CPME is less soluble in water.
②	Organic layer 93.7 Aqueous layer 4.1 Total 97.8		CPME is less soluble in water.

(3) Other Reactions-1

The following reactions in CPME proceeded similarly to those in THF.

① Synthesis of compound -2

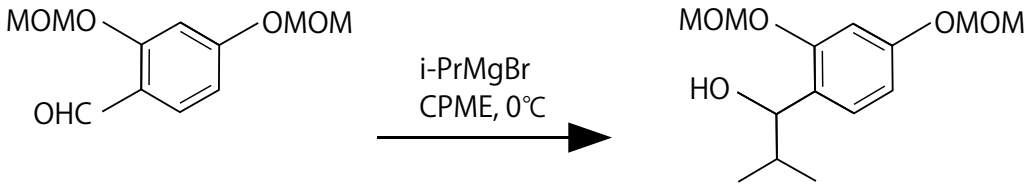
Compound 1 (5.2 mg, 9.04 μmol) was dissolved in 200 μL of CPME in a nitrogen atmosphere and cooled to -78°C. Then 15.5 μL (17.7 μmol) of 1.14-M methyl lithium in diethyl ether solution was added dropwise and the reaction mixture was stirred for 5 minutes.



Compound -1 Compound -2

② Synthesis of compound -4

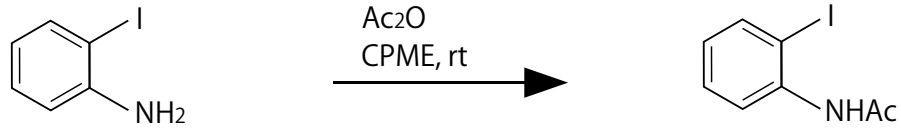
Compound 3 (21.2 mg , 94.0 μmol) was dissolved in 400 μL of CPME in an argon atmosphere and cooled to 0°C. Then 190 μL (190 μmol) of 1.00-M isopropyl magnesium bromide in THF was added as the reaction mixture was stirred for 30 minutes at 0°C.



Compound -3 Compound -4

③ Synthesis of compound -6

Compound 5 (9.7 mg, 44.3 μmol) was dissolved in 194 μL of CPME in an argon atmosphere. Acetic anhydride (45.2 μL, 443 μmol) was added, and the reaction mixture was allowed to stand for 40 minutes at room temperature.

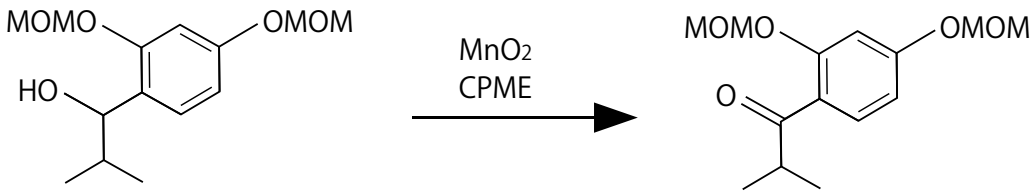


Compound -5 Compound -6

④ Synthesis of compound -8

Compound 7 (10 mg, 36.9 μmol) was dissolved in 300 μL of CPME.Then 100 mg of active manganese dioxide was added. The reaction mixture was allowed to stir for 12 hours at 50°C.

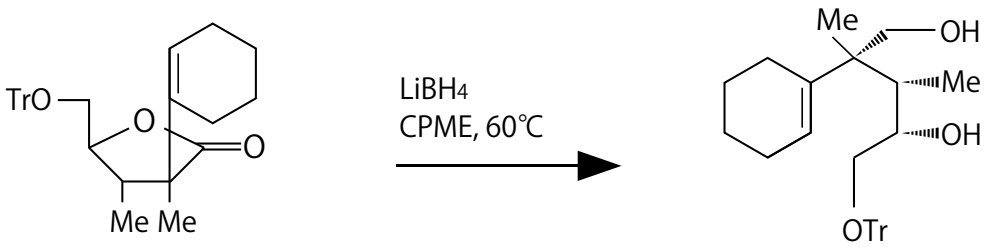
Results: The reaction proceeded until the ratio of raw materials/target materials = 1/1, regardless of whether THF or CPME was used as the solvent.
With CPME, after additional stirring for 12 hours at 95℃,
the reaction proceeded until the ratio of raw materials/target materials = 1/9.



Compound -7 Compound -8

⑤ Synthesis of compound -10

Compound 9 (60.9 mg, 131 μmol) was dissolved in 1.2 mL of CPME in an argon atmosphere and cooled to 0° C. Then 11.8 mg (522 μmol) of lithium borohydride was added, and the reaction mixture allowed to stir for 12 hours at 60° C.



Compound -9 Compound -10

(4) Other Reactions-2

In the following reactions in CPME, almost the same or better results were obtained in comparison with those in the other solvents.

1. Higher optical purity or selectivity were observed

- Asymmetric Michael alkylation
- Michael addition of R_2CuLi
- Alkylation of chiral amide
- Glycosylation
- Asymmetric hydrogenation of $NaBH_4$
- Hydrosilylation by Ru cat

2. Nucleophilic Reactions

- Amide synthesis by the reaction of acid chloride with amine
- Sillylation and desillylation
- Reaction of carbanion with aldehyde
- Debenzylation
- Alkylation of amine
- Selective methylation of phenols
- Bromination of alcohol with PBr_3
- Sulfonylchloride synthesis by the reaction of sulfonic acid with PCl_5

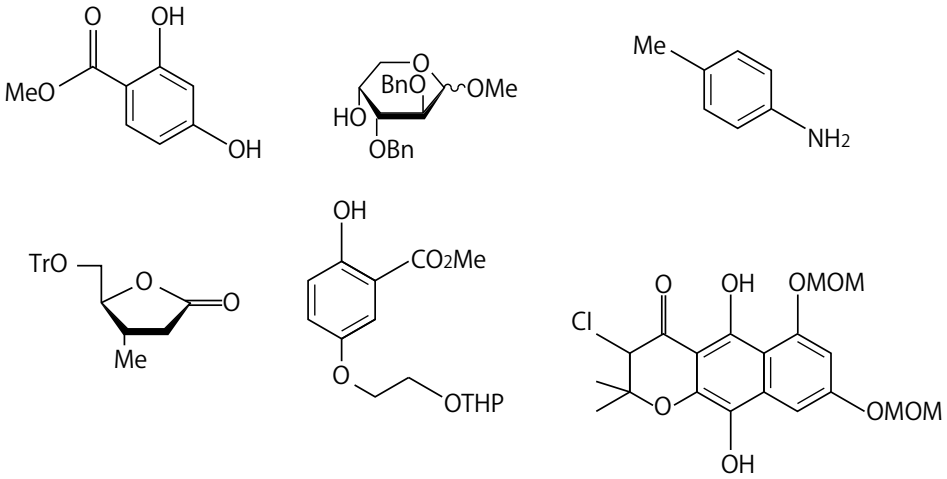
3. Reactions using metals

- Reaction of Ketone with $NaBH_4$
- Reaction of acetylenes with $Ti(OR)_4$
- Reaction using n-BuLi or Lithium Diisoprpyl Amide
- Radical cyclization of trichloroacetate using Cu cat
- Reduction of Ethyl benzoate using Lithium Aluminium Hydride
- Formation of sodium dispersion
- Intramolecular ene reaction using $ZnCl_2$

12 Extractions

1. CPME showed superior extraction performance to Diethyl Ether when evaluated with the following 6 compounds.

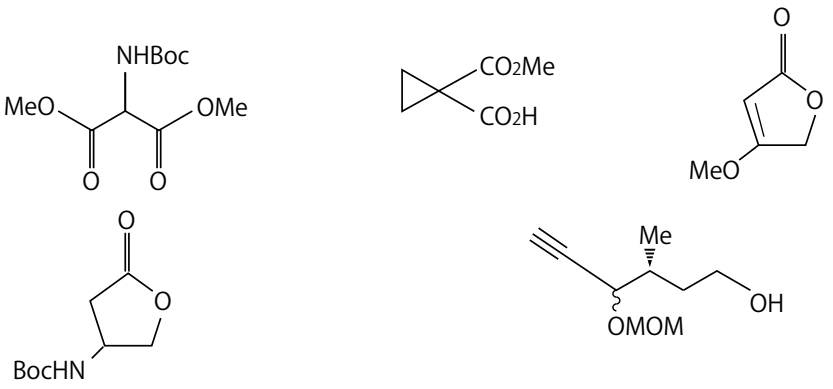
● 2 grams of each compound was dissolved in 20mL of CPME or 40mL of diethyl ether, respectively, 10mL of distilled water was added, and liquid−liquid separation was carried out.



＊Under these conditions, one extraction results with 20ml CPME gave results comparable to those obtained from two extractions with 40ml diethyl ether.

2. CPME showed similar extraction performance to Diethyl Ether when evaluated with the following 5 compounds.

● 2 grams of each compound was dissolved in 10mL of CPME or 10mL of diethyl ether, respectively, 10mL of distilled water was added, and liquid−liquid separation was carried out.



＊Under these conditions, one extraction results with 10ml CPME gave results comparable to those obtained from two extractions with 10ml diethyl ether.

13 Material Compatibility

Conditions:
After materials were immersed in CPME at 50℃ for 4hrs, their weight were measured.
Test pieces: 2mm×50mm×25mm

1) Effects of CPME on plastics

	Change of weight (wt%)	Appearance*
Polypropylene	6.3	Excellent
Polyethylene	3.7	Excellent
Hard polyvinylchloride	33.6	No Good
Soft polyvinylchloride	47.8	No Good
ABS resin	95.1	No Good
Polystyrene	dissolved	No Good
Phenol resin	−0.1	Fair
Epoxy resin	0.7	Fair
Polyacetal	−0.5	Fair
Nylon 66	−0.2	Fair
Polycarbonate	16.8	Fair
Polyacrylate	1.3	Fair
Polyurethane	78.4	Fair
Polyphenylensulfide	0.0	Excellent
PTFE	0.0	Excellent

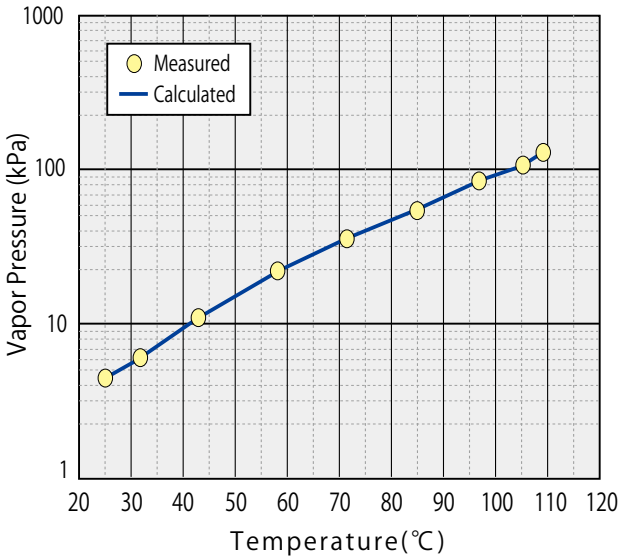
2) Effects of CPME on Rubbers

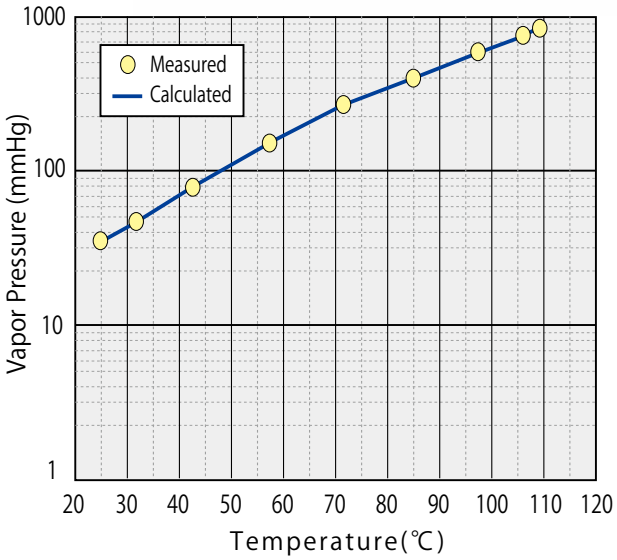
	Change of weight (wt%)	Appearance*
SBR (styren-butadiene)	94	No Good
BR (butadiene)	100<	No Good
NBR (nitrile-butadiene)	44.0	No Good
Chloroprene rubber	84	No Good
Hydrogenated NBR	62.0	No Good
Silicone rubber	100<	No Good
Fluorinated rubber	10.7	Fair

***Appearance**

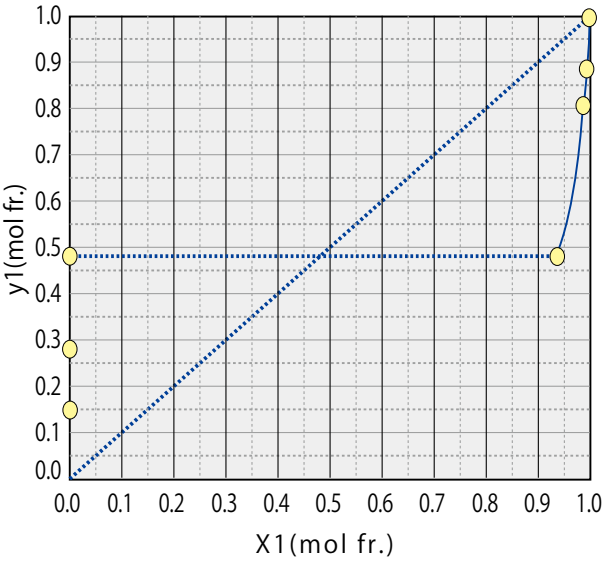
Excellent	No change
Good	Slight swelling without notable change
Fair	Swelling without notable change
No Good	Notable swelling, cracking of materials or Dissolution to CPME

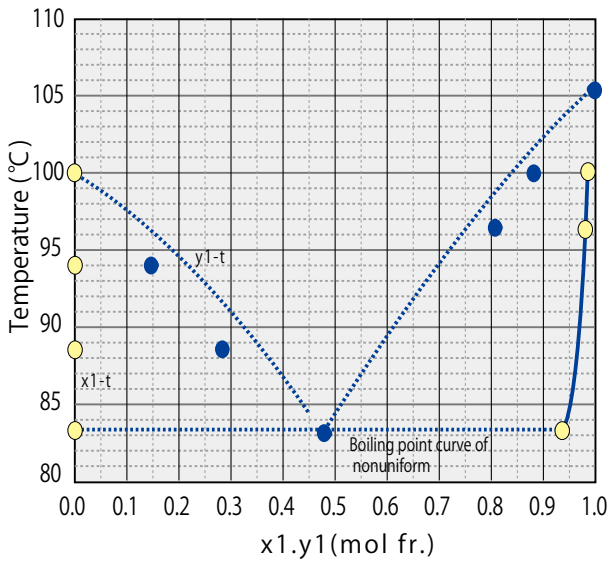
14 Vapor Pressure





15 Vapor-liquid Equilibrium of Water-CPME





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