ORIGINAL

Study on the Antioxidative Activity of 1, 3-Dioxaindan Derivatives. III.

Antioxidative Activity of 2-Alkyl-5-*t*-Butyl- 2-Methyl-1, 3-Dioxaindan

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The authors previously reported 2-alkyl-2-methyl-1, 3-dioxaindans to possess antioxidative activity even though they have no phenolic hydroxyl group. In this paper, 2-alkyl-5-*t*-butyl-2-methyl-1, 3-dioxaindans were prepared by reactions of *t*-butyl catechol with ketones in the presence of *p*-toluenesulfonic acid so as to examine effect of the introduction of a bulky *t*-butyl group at 5-position on the antioxidative activity of 2-alkyl-2-methyl-1, 3-dioxaindan.

These compounds were added to lard whose AOM stability was subsequently determined. The antioxidative activity of 2-alkyl-5-*t*-butyl-2-methyl-1, 3-dioxaindans was found to exceed that of 2-alkyl-2-methyl-1, 3-dioxaindans.

1 Introduction

Sesamol (5-hydroxy-1, 3-dioxaindan) which was formed from sesamolin during the processing of sesame seed oil is one of the most potent antioxidants. It is also known that sesamol has antimicrobial activity against some bacteria and fungi.

The antioxidative and antimicrobial activities of sesamol had been considered to be caused by the phenolic hydroxyl group in its molecule. However, the authors supposed that not only the phenolic hydroxyl group but methylenedioxy group is also responsible to these activities of sesamol, and have been working on the relation between the structures of 1, 3-dioxaindan derivatives and their activities^{1)~6)}.

In the previous papers, several 2, 2-dialkyl-1, 3-dioxaindans were prepared and their antioxidative and antimicrobial activities were examined. It was observed that these compounds have the effect to prevent the autoxidation of lard although they do not have phenolic hydroxyl group. However, these effects were not so potent as that of sesamol^{7), 8)}.

In this paper, 2-alkyl-5-*t*-butyl-2-methyl-1, 3-dioxaindans were synthesized and the enhancement of the antioxidative activities by the intro-

duction of bulky *t*-butyl group onto the aromatic ring of 2-alkyl-2-methyl-1, 3-dioxaindans was examined.

2 Experimental and Results

2.1 Materials

Ketones used for the preparation of 1, 3-dioxaindan derivatives were provided by Chisso Corporation, 4-*t*-butyl-1, 2-benzenediol (*t*-butylcatechol) was purchased from a commercial source. Lard containing no antioxidant was provided by Miyoshi Oil & Fat Co., Ltd. and used for the evaluation of antioxidative potency.

2.2 Syntheses of 2-alkyl-5-*t*-butyl- methyl-1, 3-dioxaindans

Syntheses of 2-alkyl-5-*t*-butyl-2-methyl-1, 3-dioxaindans were performed by the reaction of *t*-butylcatechol with alkyl methyl ketones according to Hartman⁹⁾. Structures and abbreviations of the compounds synthesized in this work are shown in **Table-1**.

Synthesis of 2-ethyl-5-*t*-butyl-2-methyl-1, 3-dioxaindan was carried out as follows. *t*-Butylcatechol (16.7 g) and 2-butanone (14.4 g) were dissolved in 100 mL of benzene, and 0.3 g of *p*-toluenesulfonic acid was added. The resulting solution was refluxed for 5 h removing the water formed. Then the reaction mixture was cooled

Table-1 Structures and abbreviations of 2-alkyl-5-*t*-butyl-2-methyl-1,3-dioxaindans and the compounds without 5-*t*-butyl group.

Structure		Abbreviation	
		$R_1 : -C(CH_3)_3$	$R_1 : -H$
$R_2 : -CH_3$	<i>t</i> B-MM	MM
	$R_2 : -CH_2CH_3$	<i>t</i> B-ME	ME
	$R_2 : -CH_2CH_2CH_3$	<i>t</i> B-MP	MP
	$R_2 : -CH(CH_3)_2$	<i>t</i> B-MiP	MiP
	$R_2 : -CH_2(CH_2)_2CH_3$	<i>t</i> B-MB	MB
	$R_2 : -CH_2CH(CH_3)_2$	<i>t</i> B-MiB	MiB
	$R_2 : -C(CH_3)_3$	<i>t</i> B-MtB	MtB
	$R_2 : -CH_2(CH_2)_3CH_3$	<i>t</i> B-MA	MA

Table-2 ^{13}C -NMR data of 2-ethyl-5-*t*-butyl-2-methyl-1,3-dioxaindan.

Signal(ppm)	Structure
a : 147.700 b : 145.457 c : 144.628 d : 119.372 e : 117.129 f : 107.280 g : 106.061 h : 34.633 i : 32.341 j : 31.756 k : 23.809 l : 7.722

and washed with water. After the removal of the solvent the product was isolated by distillation under reduced pressure. The distillate was refined through silica gel column using benzene/hexane-95/5(vol/vol) as the eluting solvent.

Other 2-alkyl-5-*t*-butyl-2-methyl-1,3-dioxaindans were synthesized in similar procedures using *t*-butylcatechol and corresponding ketones, and refined by the same way as above.

The elementary analyses and the ^{13}C -NMR spectroscopic determination of the products were carried out. The results of the elementary analyses were agreed with the calculated values. ^{13}C -NMR data of 5-*t*-butyl-2-ethyl-2-methyl-1,3-dioxaindan are shown in **Table-2**. These analytical data supported the structure of this compound. Similar results were obtained for the other

compounds. From the results of elementary analyses and ^{13}C -NMR spectroscopic determination it was confirmed that the reaction products were 2-alkyl-5-*t*-butyl-2-methyl-1,3-dioxaindans.

2.3 Evaluation of antioxidative potency

The antioxidative activities of 2-alkyl-5-*t*-butyl-2-methyl-1,3-dioxaindans were determined as follows.

AOM stability of the lard containing each compound in 0.05% was determined according to the Official Method of the Japan Oil Chemists' Society 2.4.28.1-81. **Fig.-1** shows the change of the peroxide values of the lard during the AOM test. The AOM stabilities of the samples were read from these curves as the time required to attain 100 meq/kg of peroxide value.

Fig.-1 AOM tests of the lard containing 2-alkyl-5-*t*-butyl-2-methyl-1,3-dioxaindan.

Antioxidation factor of each compound added to the lard was calculated from the AOM stability of the sample according to Kovats¹⁰⁾. The antioxidation factors of 2-alkyl-5-*t*-butyl-2-methyl-1,3-dioxaindane are shown in Table-3. Those of 2-alkyl-2-methyl-1,3-dioxaindane which were previously reported^{7),8)} are also shown in Table-3 for the comparison.

3 Discussion

In the previous paper, the authors reported that 2-alkyl-2-methyl-1,3-dioxaindane have antioxidative activities although they do not have phenolic hydroxyl group. The antioxidation factors of 2-alkyl-2-methyl-1,3-dioxaindane corre-

lated well with the chemical shifts (δ -values) of the carbons at 2-positions of these compounds as shown in Table-3. So it was supposed that radical scavenging activities of these compounds arose by the increase of the electron densities at 1- and 3-positions caused by the electron donating effect of alkyl substituents at 2-position.

In the present work, the antioxidative activities of 2-alkyl-5-*t*-butyl-2-methyl-1,3-dioxaindane were higher than those of 2-alkyl-2-methyl-1,3-dioxaindane. It was considered that radical scavenging activities were enhanced by the introduction of *t*-butyl group at 5-position. Especially, the antioxidation factors of *t*B-MtB and *t*B-MtB were nearly as high as that of sesamol. The chemical shifts of ¹³C-NMR signals of the carbons at 2-positions of the compounds synthesized appeared in the lower field compared with those of 2-alkyl-2-methyl-1,3-dioxaindane. However, correlation between the antioxidation factor and the chemical shifts of 2-carbons was not found as shown in Table-3. It was supposed that by the introduction of bulky *t*-butyl group the solubilities of these compounds in the lard differed significantly, and the antioxidation activities were affected not only by the electron densities at 2 and 1,3 positions but also by the solubilities. It will be necessary to increase the solubility in the

Table-3 Antioxidative activities and signal in the ¹³C-NMR spectrum attributed to the 2-position carbon of 2-alkyl-5-*t*-butyl-2-methyl-1,3-dioxaindane compared with those of the compounds without 5-*t*-butyl group.

Compound	AOM stability(h)*	Antioxidation factor**	Signal (ppm)	Compound	Antioxidation factor**	Signal (ppm)
<i>t</i> B-MM	29.0	4.14	117.422	MM	1.48	117.373
<i>t</i> B-ME	40.0	5.71	119.372	ME	2.13	119.226
<i>t</i> B-MP	54.5	7.79	119.031	MP	2.06	118.982
<i>t</i> B-MtP	26.8	3.83	121.273	MtP	2.41	121.225
<i>t</i> B-MB	52.5	7.50	119.128	MB	1.81	119.079
<i>t</i> B-MtB	71.5	10.21	119.274	MtB	2.75	119.177
<i>t</i> B-MtB	75.0	10.71	122.980	MtB	4.44	122.931
<i>t</i> B-MA	13.5	1.93	119.128	MA	1.38	119.177

* AOM stability of the lard containing 2-alkyl-5-*t*-butyl-2-methyl-1,3-dioxaindane or 2-alkyl-2-methyl-1,3-dioxaindane.

** Antioxidation factor =
$$\frac{\text{AOM stability of the lard containing 2-alkyl-5-}t\text{-butyl-2-methyl-1,3-dioxaindane or 2-alkyl-2-methyl-1,3-dioxaindane.}}{\text{AMO stability of the lard}}$$

oil for enhancement of the antioxidative activity.

Acknowledgment

The authors appreciate Chisso Corporation and Miyoshi Oil & Fat Company for providing materials.
(Received Mar. 9, 1990)

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1, 3-ジオキサインダン誘導体の 酸化防止力(第3報)

2-アルキル-5-*t*-ブチル-2-メチル-1, 3-
ジオキサインダンの酸化防止力

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著者らは前報で、2-アルキル-2-メチル-1, 3-ジオキサインダンが分子内にフェノール性ヒドロキシル基を持たないにもかかわらず、油脂に対する酸化防止力を持つことを報告した。本報では、*t*-ブチルカテコールとケトンとの反応により 2-アルキル-5-*t*-ブチル-2-メチル-1, 3-ジオキサインダンを合成し、2-アルキル-2-メチル-1, 3-ジオキサインダンの 5 位へのバルキーな *t*-ブチル基の導入による酸化防止力への影響を調べた。

2-アルキル-5-*t*-ブチル-2-メチル-1, 3-ジオキサインダンをラードに添加し AOM 安定度を測定した。その結果、これらの化合物には 5 位に *t*-ブチル基を持たない化合物に比較し、より強い酸化防止力が認められた。