NBS-Promoted Reactions of Symmetrically Hindered Methylphenols via *p*-Benzoquinone Methide

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Symmetrically hindered methylphenols **1** react smoothly with NBS to form transient intermediates, *p*-benzoquinone methides (BM), which can be further processed to give hydroxybenzaldehydes in the presence of DMSO. This reaction is initiated by the formation of the phenoxy radical, followed by disproportionation to afford BM. None of the side-chain-brominated product is observed. The existence of BM is supported by the following observations: the formation of BM in solution can be monitored by GC and GC−MS; the electrophilic methine part participates in electrophilic aromatic substitution with anisoles to give hydroxybenzylated products **15**; and the double bond character of the exocyclic methine plays a role in [4 + 2] cycloaddition with diene to afford Diels−Alder adducts. In contrast, unsymmetrically hindered or simple methylphenol (*p*-cresol) with NBS gives the nuclear brominated products, as usual. The energies of symmetrically hindered BMs, unsymmetrically hindered BM, and simple BM were calculated using density functional theories. Relative stabilization energies calculated at the B3LYP/6-31G*//B3LYP/6-31G* level by an isodesmic equation are enhanced 3−6 kcal/mol for symmetrically hindered BMs.

Introduction

Reactive benzoquinone methides have received considerable attention since these intermediates were shown to be involved in the oxidation of phenols[1] and in the biosynthesis of neolignans.[2] The *p*-benzoquinone methide **A** without a substituent on the methide part is highly reactive, which can be explained by another resonance structure **B** with a dipolar character that shows an electrophilic property on its methine terminus. Thus, the double bond and electrophilic characters of the exocyclic alkylidene carbon have been exploited both in typical Diels−Alder reactions with dienes[3] and in 1,6-additions with nucleophiles,[4] such as phosphites,[4a] phosphines,[4b] amines,[4c] or phenoxides,[4d] as a result of the additional driving force of aromatization after conjugated addition. However, the *p*-benzoquinone methides only exist transiently in dilute solution. Therefore, they usually cannot be isolated, although they may be detectable by spectroscopy.[5] The application of these highly reactive intermediates in reactions with a wide variety of nucleophiles is limited by their stability and the methods used for their generation.[6] Even though the same *p*-benzoquinone methide can be generated by different methods, the same reactions may not take place with a nucleophile because of the difference in chemical environments. These unusual results with benzoquinone methides have been described elsewhere.[7] However, *p*-benzoquinone methides with substituents on the terminal methylene (structure **C**) can be isolated, and intramolecular electrophilic substitution reactions have been well studied by Angle and co-workers.[8]

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(6) A few methodologies have so far been developed to generate 2,6-di-*tert*-butylquinone methide in situ: (a) oxidation of 2,6-di-*tert*-butyl-*p*-cresol with Ag_2O[5,7a] or PbO_2, also see Bolon, D. A. *J. Org. Chem.* **1970**, *35*, 715. Orlando, C. M. *J. Org. Chem.* **1970**, *35*, 3714. Hill, J. H. L. *J. Org. Chem.* **1967**, *32*, 3214. Becker, H. D.; Gustafson, K. *J. Org. Chem.* **1976**, *41*, 214; (b) treatment of 2,6-di-*tert*-butyl-4-hydroxybenzyl bromide with triethylamine;[5,15b] (c) thermal decomposition of (4-hydroxy-3,5-di-*tert*-butylbenzyl)trimethylammonium iodide generated from Mannich base and CH_3I;[3c,4e,f] and (d) treatment of 4-(benzotriazol-1-ylmethyl)-2,6-di-*tert*-butylphenol with base.[4f]

(7) 2,6-Di-*tert*-butylbenzoquinone methide **3a** generated from 3,5-di-*tert*-butyl-4-hydroxybenzyl chroride with triethylamine reacts with triethyl phosphite to afford bisphenol as a major product along with 2−5% of phosphonate. However, **3a** prepared by the thermal decomposition of Mannich base and CH_3I, reacts with triethyl phosphite to give phosphonate in 95% yield. See ref 4a and Dubs, P.; Stegmann, W.; Luisoli, R.; Martin, R. EP 434606 A1 910626; *Chem. Abstr. 115*, 136390.

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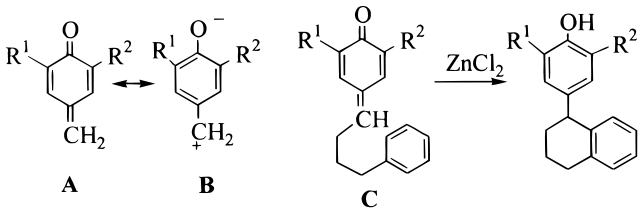
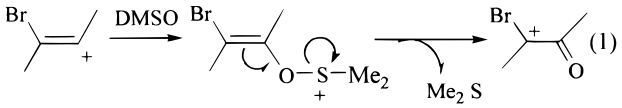


Recently, we developed new methods for intermolecular electrophilic aromatic substitution with a transient 2,6-di-*tert*-butylbenzoquinone methide generated in situ from the thermal decomposition of Mannich base−$(MeO)_2SO_2$ and for the easy detection of the formation of transient benzoquinone methide with GC−MS.[9] Our interest in the reactions of *p*-benzoquinone methides **A** has prompted us to examine various reactions for in situ preparation and electrophilic addition. In particular, we have been interested in trapping the conjugated methine part of **A** by an oxygen nucleophile. Dimethyl sulfoxide (DMSO) as the nucleophilic oxygen donor has been used in the oxidation of several different functional groups: (i) in bromohydrin formation with olefins via the incorporation of oxygen to bromocarbonium ion,[10] (ii) in benzil formation with diphenylacetylene via the oxidation of a vinyl cation,[11] (iii) in the conversion of benzyl bromides to benzaldehydes,[12] (vi) in Pfitzner−Moffatt oxidation,[13] etc. The nucleophilic oxygen of DMSO may be associated with the exocyclic alkylidene carbon of **A**. A similar behavior is observed for a vinyl cation in the oxidation of acetylenes by DMSO to give oxysulfonium cation (eq 1).[11]

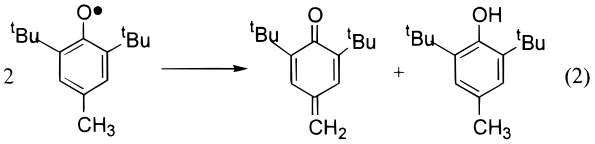


In adapting the DMSO reagent to this new use, we systematically examined several known methods[6] for preparing transient intermediates to lead to oxidation. Our initial investigations focused on the direct oxidation of methyl substituents to formyl groups in sterically hindered phenols. As expected, the oxidation of 2,6-di-*tert*-butylbenzoquinone methide **3a** generated in situ by a well-known method, i.e., oxidation of 2,6-di-*tert*-butyl-4-methylphenol **1a** by Ag_2O,[6a] took place when we added DMSO to produce 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde **2a**. Unfortunately, the best yield we obtained was 26%, and dimerization of *p*-benzoquinone methide was the major reaction pathway. In fact, these results prompted a continuing study of the effects of *p*-benzoquinone methides on the performance of DMSO as an oxygen donor. We did not think that the use of Ag_2O would help to increase the yield of hydroxybenzaldehydes. Thus, we chose NBS as an effective oxidant for driving the reaction because of the chance of H abstraction in phenols by a succinimidyl radical.[14] After the phenoxy radical is generated, it is rapidly disproportionated to *p*-benzoquinone methide and phenol, as shown in eq 2.[15] We report here the successful formation of symmetrically hindered *p*-benzoquinone methides and ab initio calculations for their stabilization energies.

Table 1. Oxidation of 2,6-Di-*tert*-butyl-4-methylphenol under various conditions[a]

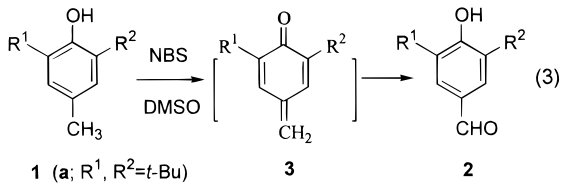
entry	promoter	solvent	conditions	additive	yields (%)[b]
1	NBS	DMSO	120 °C, 10 min	none	**2a** (95)
2	NBS (0.2 equiv)	DMSO	120 °C, 3 h	none	**2a** (89)
3	I_2	DMSO	120 °C, 24 h	none	**2a** (10) **1a** (29)
4	$COCl_2$	DMSO	120 °C, 24 h	none	**2a** (tr) **1a** (29)
5	NBS	CCl_4	reflux, 4h	none	**3a** (69) **1a** (29)
6	NBS	CCl_4	reflux, 24h	BP[c]	**3a** (95)
7	NBS	CCl_4	reflux, 24h	DMSO	**2a** (78) **3a** (11)
8	NBS	CCl_4 + DMSO	120 °C, 3 h	none	**2a** (91)

[a] Reactions were performed using **1a** (1.0 mmol) and 1.2 equiv of promoter in 10 mL of DMSO. [b] The product distributions in all cases were determined by GLC with an internal standard. [c] 0.1 equiv of benzoyl peroxide was added.



Results and Discussion

(1) Oxidation of *p*-Benzoquinone Methides. 2,6-Di-*tert*-butyl-4-methylphenol **1a** (1 mmol) with NBS (1.2 mmol) in DMSO solution at 120 °C afforded 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde **2a** in a quantitative yield (eq 3, Table 1). The oxidation of **1a** was completed within



10 min, and neither further oxidation to carboxylic acid nor hydroxybenzyl bromide formation was observed. This procedure offers significant advantages over the Duff reaction and the Reimer−Tiemann formylation of phenols, each of which gives low yields under harsh conditions and sometimes requires the use of toxic reagents.[16] Furthermore, the direct oxidation of *p*-alkylphenols for the synthesis of *p*-carbonylphenols with common oxidants was reported to be unsuccessful.[17]

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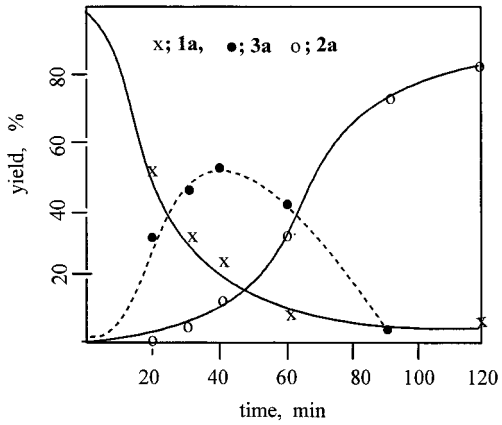
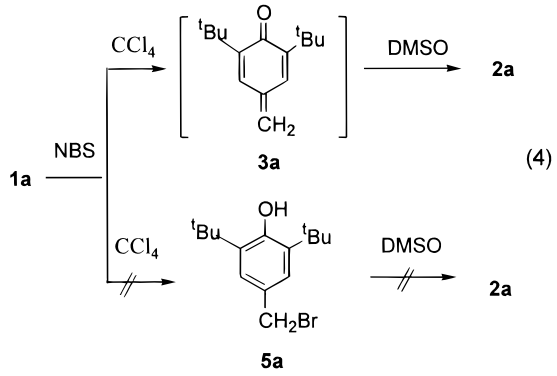


Figure 1. Time/course profile for the reaction of **1a** and NBS in DMSO (initial concentrations 0.1 and 0.02 M, respectively).

The reaction proceeded by consuming either stoichiometric or catalytic amounts of NBS. For example, oxidation of **1a** with 0.2 equiv of NBS led to product **2a** in 89% yield and recovered **1a** in 6% yield (entry 2) as well as the stoichiometric reaction (entry 1). The catalytic reaction proceeded slowly but was completed in 3 h. Surprisingly, in this case, we observed the formation of a transient intermediate, 2,6-di-*tert*-butylbenzoquinone methide **3a**, during the transformation of **1a** to **2a**, and we did not observe any traces of a halogenated phenol. Evidence for the formation of **3a** in the reaction of **1a** with NBS is presented in Figure 1. Monitoring of this reaction by GC showed that the decrease in **1a** was counterbalanced by a favorable trend in the sum of **3a** and **2a**, which increased steadily until a certain point. After ~50% of **3a** was generated in situ in solution, the transient intermediate *p*-benzoquinone methide gradually disappeared from the reaction mixture, and eventually the sole product **2a** was isolated in 89% yield. However, the oxidation of **1a** to **2a** with a stoichiometric amount of NBS occurs so fast that the *p*-benzoquinone methide **3a** is not detected. We were led to the use of I_2 instead of NBS by a related report on the conversion of methylpyridines to pyridine aldehydes with I_2/DMSO.[18] According to that report, methylpyridine−I_2 complex was heated to form iodomethylpyridine, which was then reacted with DMSO to give pyridine aldehyde via oxydimethyl sulfonium iodide. However, in the case of I_2 or $COCl_2$, **1a** was oxidized in only trace amounts to form **2a**, and most of the starting material was recovered (entries 3 and 4). None of the halogenated products was observed during the reactions.

To reinvestigate the halogenation of alkylphenols more thoroughly, we examined the bromination of **1a** with NBS in CCl_4 in either the absence or the presence of benzoyl peroxide (entries 5 and 6). Surprisingly, neither 3,5-di-*tert*-butyl-4-hydroxybenzyl bromide **5a** nor the oxidized product **2a** was observed. Instead, we observed the formation of *p*-benzoquinone methide **3a**. After the formation of **3a** was complete, DMSO was added, and the reaction mixture was heated for an additional 24 h (entry 7, eq 4). The oxidized product **2a** was formed in 78% yield.



Furthermore, the oxidation reaction of **1a** with NBS proceeded to produce **2a** in a solution of CCl_4−DMSO (entry 8). The formation of **2a** from **3a** in entries 7 and 8 suggests that the oxidation proceeds via a *p*-benzoquinone methide in DMSO.

In an attempt to prove that the brominated methylphenol intermediate is not involved in the oxidation of 2,6-di-*tert*-butyl-4-methylphenol **1a** with NBS, we tried to oxidize isolated 3,5-di-*tert*-butyl-4-hydroxybenzyl bromide[3b] **5a** in DMSO solution without NBS at 120 °C (eq 4). However, the DMSO oxidation of 3,5-di-*tert*-butyl-4-hydroxybenzyl bromide **5a** did not occur even under these vigorous conditions. Furthermore, simple hydroxybenzyl bromides, such as *p*-hydroxybenzyl bromide, were not oxidized at all, although the benzyl halide can be oxidized to the benzaldehyde by DMSO.[12] An important feature of the reaction pathways is that 3,5-di-*tert*-butyl-4-hydroxybenzyl bromide **5a** is not involved as an intermediate in the NBS−DMSO oxidation of 2,6-di-*tert*-butyl-4-methylphenol.

The mechanism of the conversion of 2,6-di-*tert*-butyl-4-methylphenol **1a** to 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde **2a** could involve both radical initiation by NBS and oxidation by DMSO (Schemes1 and 2). 2,6-Di-*tert*-butyl-4-methylphenoxy radicals **6** are readily generated by the oxidation of one electron of its phenol, and the resulting phenoxy radicals **6** disproportionate rapidly to yield the parent phenol **1a** and *p*-benzoquinone methide **3a**.[15] Alternatively, a positive bromine attacks phenol to form a hypobromite **7**, which readily forms *p*-benzoquinone methide **3a**, and hydrogen bromide may be liberated by spontaneous dehydrobromination. Meanwhile, bromodimethylsulfonium bromide **8** would be readily generated in situ from HBr in DMSO (eq 5).[19]

(16) To achieve formylation of phenols, HCN−$AlCl_3$, aqueous NaOH, or $C_6H_{12}N_4$ is referred to as the reagent of choice. However, yields are poor to fair, and low regioselectivities have been observed. For example, the Duff reaction of 2,6-dimethoxyphenol gives **2b** in 31% yield. For a representative example, see: Larrow, J. F.; Jacobsen, E. N.; Gao, Y.; Hong, Y.; Nie, X. *J. Org. Chem.* **1994**, *59*, 1939.

(17) Most commonly used oxidants for the oxidationof methyl groups on aromatic rings are cerium(IV), *tert*-butyl hydroperoxide with catalysts, acetone cyanohydrin−$AlCl_3$, chromium(VI), and O_2 with enzymes. Even though a number of methods are currently available, attempts to achieve the direct oxidation of hindered methylphenols to hydroxybenzaldehydes are met with difficulties. For example, methyl-substituted aromatic systems can be oxidized cleanly to a single aldehyde with ceric ammonium nitrate (CAN); however, toluenes with strongly electron-donating substituents such as hydroxy, alkoxy, or amino polymerize during the oxidation reaction. See: Trahanovsky, W. S.; Young, L. B. *J. Org. Chem.* **1966**, *31*, 2033. Even with the O_2-enzyme lactase method, phenolic and benzylic hydroxyl groups require protection before oxidation of aromatic methyl groups. See: Potthast, A.; Rosenau, T.; Chen, C.-L.; Gratzl, J. S. *J. Org. Chem.* **1995**, *60*, 4320. For reviews on the oxidation of methylarenes to their aldehydes, see: (a) Wilberg, K. B. *Oxidation in Organic Chemistry*; Wilberg, K. B., Ed.; Academic: New York, 1965; pp 101−105. (b) Larock, R. C. *Comprehensive Organic Transformation*; VCH: New York; 1989; pp 591−592.

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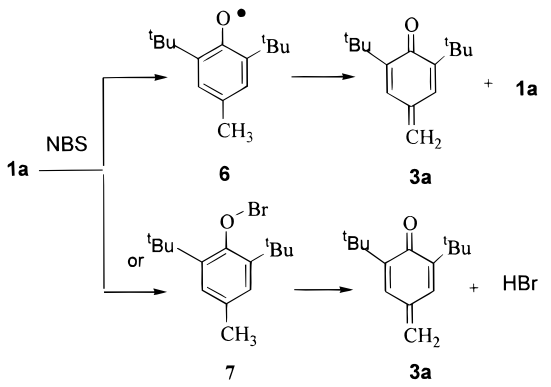
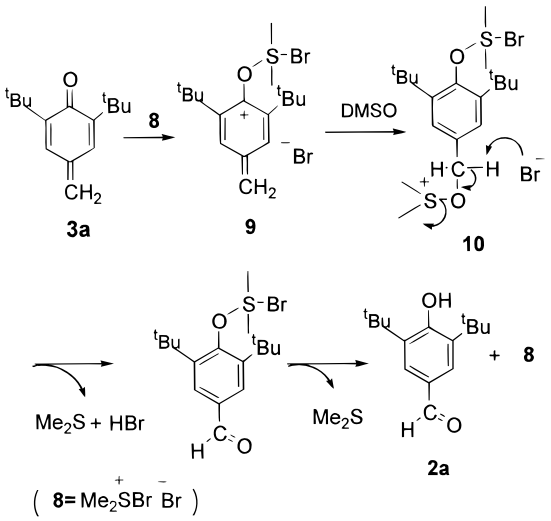
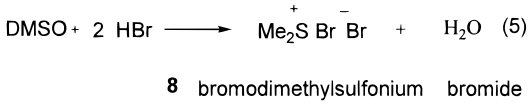
Scheme 1



Scheme 2



p-Benzoquinone methide **3a** would then rapidly react



with **8**, followed by the incorporation of DMSO to form oxydimethyl sulfonium intermediate **10**. The methine part of **3a** would be more electrophilic with the addition of bromodimethylsulfonium to the oxygen of the carbonyl of intermediate **9**. When *p*-benzoquinone methide was generated by a Ag_2O method in the absence of NBS (without the formation of **8**), the oxidation with DMSO alone occurred slowly and gave a very low yield. This may suggest that a strong activation effect by the addition of bromodimethylsulfonium bromide **8** to **3a** is important for the oxidation to occur readily. The subsequent oxidation to 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde **2a** is undoubtedly similar to the Pfitzner−Moffatt mechanism.[13]

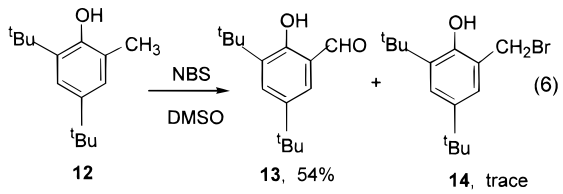
The application of NBS−DMSO oxidation to other symmetrically hindered *p*-methylphenols provided their *p*-formylphenols in over 83% yields (Table 2). The reaction proceeded smoothly to completion within 4 h. Slightly increased product yields were obtained when the *p*-methylphenols were substituted with strong electron-donating groups, such as methoxy, *tert*-butyl, or phenyl groups. Furthermore, we observed a highly regioselective mono-oxidation of 2,4,6-trimethylphenol to give a single product, 3,5-dimethyl-4-hydroxybenzaldehyde, in 83% yield (entry 5). The oxidation reaction takes place at the *para* methyl substituent to lead to the predominant formation of *p*-benzoquinone methide.

Table 2. Oxidation of Sterically Hindered *p*-Methylphenols by NBS in DMSO

	methylphenols			molar ratio		
entry	**1**	R^1	R^2	(**1**:NBS)	min	yield (%)[a]
1	**1a**	*t*-Bu	*t*-Bu	1:1.2	10	**2a** (95)
2	**1b**	OMe	OMe	1:1.1	60	**2b** (95)
3	**1c**	Ph	Ph	1:1.4	120	**2c** (93)
4	**1d**	*i*-Pr	*i*-Pr	1:1.4	240	**2d** (86)
5	**1e**	Me	Me	1:1.4	240	**2e** (83)
6	**1f**	Me	H	1:1.3	60	**11f**[b] (77)
7	**1g**	OMe	H	1:1.4	60	**11g**[b] (56)
8	**1h**	H	H	1:1.2	60	**11h**[b] (51)

[a] The product yield was determined by GLC with an internal standard. [b] Compounds **11** are *o*-brominated methylphenols.

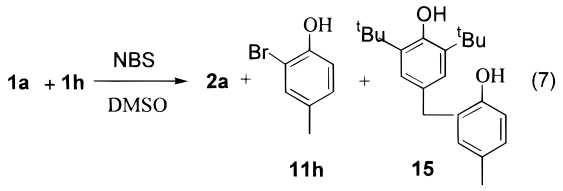
With a blocking group at the *para* position, *ortho* regioselective oxidation of *o*-methylphenols was observed. In the case of 4,6-di-*tert*-butyl-2-methylphenol **12**, which has a blocking group at the *para* position, oxidation gave 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde **13** in 54% yield. A trace amount of 3,5-di-*tert*-butyl-2-hydroxybenzyl bromide **14** was also observed by GC−MS analysis (eq 6).



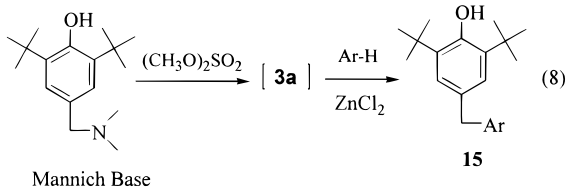
However, unsymmetrically substituted and simple *p*-methylphenols underwent nuclear bromination at the *ortho* position of *p*-methylphenols (Table 2, entries 6−8, compounds **11**). Only trace amounts of hydroxybenzaldehyde were observed. For example, in the case of *p*-cresol **1h**, oxidation to *p*-hydroxybenzaldehyde did not occur with NBS in DMSO; instead, 2-bromo-4-methylphenol **11h** and a trace of 2,6-dibromo-4-methylphenol were obtained (entry 8). Recently, Majetich and coworkers[19] observed the electrophilic aromatic bromination of strongly activated benzenes with bromodimethylsulfonium bromide **8**, generated in situ by treating DMSO with aqueous HBr. Our results using NBS were very similar to Majetich's. These results support the notion that unsymmetrically hindered or simple methylphenols react with NBS by an ionic process that involves heterolytic dissociation of the N−Br bond. However, symmetrically hindered methylphenols might be subject to the formation of a stable transient intermediate, *p*-benzoquinone methide, via a radical process. The poor results with unsymmetrically substituted *p*-methylphenols using NBS−DMSO promopted us to examine the competition between oxidation and nuclear bromination. An equimolar mixture of **1a** and **1h** with NBS (1 equiv) in DMSO under the same reaction conditions gave **2a** (39%), **11h** (43%), and **15** (5%) (eq 7).

The hydroxybenzylated adduct **15** is produced by way of the intermolecular electrophilic substitution of *p*-cresol with 2,6-di-*tert*-butylbenzoquinone methide. As previ-

(19) Majetich, G.; Hicks, R.; Reister, S. *J. Org. Chem.* **1997**, *62*, 4321. The mechanism accounts for the formation of bromomethylsulfonium bromide **8** from DMSO and HBr, see: Mislow, K.; S. Mmons, T.; Melillo, J.; Ternay, A. *J. Am. Chem. Soc.* **1964**, *86*, 1452.

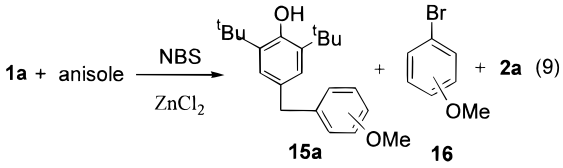


ously mentioned, the electrophilic character of the exocyclic alkylidene carbon in the transient *p*-benzoquinone methide has been considered as a potential candidate for the intermolecular substitution of arenes. From our previous results,[9] the intermolecular electrophilic aromatic substitution reaction of anisoles with *p*-benzoquinone methide generated from the Mannich base and $(CH_3O)_2SO_2$ affords the hydroxybenzylated products **15** in up to 94% yield in the presence of $ZnCl_2$ (eq 8). The



coordination of Lewis acid to an oxygen of *p*-benzoquinone methide generates the activated carbocation, which participates in the aromatic substitution reaction of arenes. Most arenes with activating substituents gave the hydroxybenzylated products **15** in reasonable to high yields. Therefore, we examined the arylation reaction of benzoquinone methide generated from NBS in CCl_4, expecting formation of an activated *p*-benzoquinone methide by $ZnCl_2$, which would lead to arenes by electrophilic substitution. In fact, the *p*-benzoquinone methide of **1a** with NBS was clearly formed in CCl_4 (Table 1, entry 5), and the activation effect by bromodimethylsulfonium bromide **8** can be eliminated because we did not use DMSO.

(2) Arylation of *p*-Benzoquinone Methides. A mixture of **1a** (5 mmol, a limiting reagent), anisole (25 mmol), and NBS (7.5 mmol) in the presence of $ZnCl_2$ (5 mmol) was heated at 120 °C in CCl_4 (30 mL) to give the hydroxybenzylated anisole **15a** in 83% yield with 86:14 *para*/*ortho* regioselectivity (eq 9). The brominated ani-



soles **16** were also produced in overall 8% yield, along with a trace amount of hydroxybenzaldehyde **2a**.

To investigate the substituent effect of arenes in the electrophilic substitution reaction with *p*-benzoquinone methide, we carried out more preliminary studies (Table 3). By changing the solvent from CCl_4 to DMSO in the presence of $ZnCl_2$, both the oxidation of **1a** and the nuclear bromination of anisole occurred, as well as hydroxybenzylation (entry 2). In the absence of $ZnCl_2$, the rate and yield of **15a** were decreased, and the yield of brominated anisoles was significantly increased in CCl_4. Attempts to increase the yield of hydroxybenzylated product by changing the solvent and Lewis acid were unsuccessful. Using CCl_4 as a solvent, $ZnCl_2$ was the most

Table 3. Intermolecular Electrophilic Substitution Reaction of Arenes with *p*-Benzoquinone Methide Generated in Situ from 2,6-Di-*tert*-butyl-4-methylphenol[a]

entry	arene	solvent	Lewis acid (equiv)	**15a** %[b]	**16,** %[c]
1	anisole	CCl_4	$ZnCl_2$ (1.5)	83	8
2	anisole	DMSO	$ZnCl_2$ (3.0)	45 (35)[d]	14
3	anisole	CCl_4	none	11	65
4	anisole	CCl_4	$AlCl_3$ (1.5)	31	35
5	phenol	CCl_4	$ZnCl_2$ (1.5)	8 (43)[e]	75
6	*p*-cresol	CCl_4	$ZnCl_2$ (3.0)	8 (55)[e]	43
7	o-anisidine	CCl_4	$ZnCl_2$ (1.0)	0	93
8	*N*,*N*-dimethyl-aniline	CCl_4	$ZnCl_2$ (3.0)	8	48
9	*N*,*N*-dimethyl-toluidine	CCl_4	$ZnCl_2$ (3.0)	45	40
10	4-bromoanisole	CCl_4	$ZnCl_2$ (1.0)	15	56
11	4-nitroanisole	CCl_4	$ZnCl_2$ (1.0)	19	29
12	*p*-xylene	CCl_4	$ZnCl_2$ (1.0)	0 (47)[e]	33

[a] Reactions were performed using **1a** (1.0 mmol) and 5 equiv of arene in 7 mL of solvent. [b] The product distributions in all cases were determined by GLC with an internal standard. [c] Overall yield of mono- and dibrominated arene. [d] 3,5-Di-*tert*-butyl-4-hydroxy benzaldehyde. [e] 2,6-Di-*tert*-butyl-4-methylphenol was recovered.

effective Lewis acid for the electrophilic substitution reaction of *p*-benzoquinone methide. A limitation of this reaction was found with very strongly activated arenes, indicating that NBS acted as a brominating reagent rather than as an oxidant, and the phenolic compounds are more susceptible to bromination than other examples. Thus, the reaction of phenol with NBS in CCl_4, carried out under the same conditions, gives the nuclear brominated product contaminated with a small amount of dibrominated phenols. In addition to the nuclear bromination by NBS, the free-radical side-chain brominations of arenes could be a possible route in the presence of NBS. However, the side-chain bromination of *p*-cresol does not occur. Several groups have recognized that nuclear bromination of phenols and anisoles with NBS is greatly favored over side-chain bromination in propylene carbonate,[20a] CH_3CN,[20b–d] CS_2,[20c] DMF,[20f] or CCl_4.[20g,h] Despite the apparent utility of NBS, it has not been widely used for the halogenation of arenes in DMSO.[21]

It is also known that reactions with NBS are strongly affected by changing the substituents on the arene and the solvent. Contrary to the strongly activated arenes, the electrophilic substitution reactions of arenes with moderately activating substituents, such as *N*,*N*-dimethyltoluidine, proceed to react with *p*-benzoquinone methide to give the hydroxybenzylated products (entry 9). Meanwhile, hydroxybenzylation was very sluggish with electron-withdrawing-group-substituted anisoles. Inactivated arenes, such as toluene, xylene, or methyl-

(20) The nuclear bromination of activated aromatic compounds (phenols, anisoles) with NBS is clearly favored by polar solvents such as propylene carbonate: (a) Ross, S. D.; Finkelstein, M.; Petersen, R. C. *J. Am. Chem. Soc.* **1958**, *80*, 4327. Nuclear bromination in CH_3CN: (b) Oberhauser, T. *J. Org. Chem.* **1997**, *62*, 4505. (c) Carreno, M. C.; Ruano, J. L.; Sanz, G.; Toledo, M. A.; Urbano, A. *Synlett.* **1997**, 1241. (d) Carreno, M. C.; Ruano, J. L.; Sanz, G.; Toledo, M. A.; Urbano, A. *J. Org. Chem.* **1995**, *60*, 5328. Nuclear bromination in DMF: (e) Michell, R. H.; Lai, Y.; Williams, R. V. *J. Org. Chem.* **1979**, *44*, 4733. The nuclear versus side-chain bromination of anisoles with NBS in CCl_4 is also well documented, see: (f) Gruter, G. M.; Akkerman, O. S.; Bickelhaupt, F. *J. Org. Chem.* **1994**, *59*, 4473. (g) Goldberg, Y.; Bensimon, C.; Alper, H. *J. Org. Chem.* **1992**, *57*, 6374.

(21) The site-selective bromination of arenes with aqueous HBr in DMSO has recently been reported. However, this report lacks of the varsity of arenes, and no example with NBS is appeared. See: Srivastava, S. K.; Chauhan, P. M. S.; Bhaduri, A. P. *J. Chem. Soc., Chem. Commun.* **1996**, 2679.

Table 4. Electrophilic Substitution Reaction of Anisoles with 2,6-dialkyl-4-methylphenols[a]

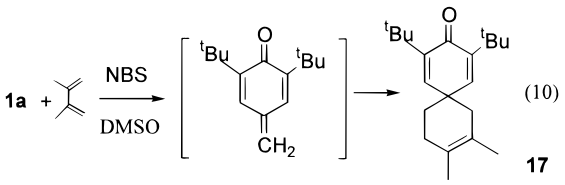
						products, %[b]		
entry	**1**	anisoles	NBS (equiv)	$ZnCl_2$ (equiv)	time (h)	**15** (*o*/*p*)	**2**	**16**[c]
1	**1a**	anisole	1.5	1.0	10	83 (86/14)	0	6
2	**1b**	*p*-methylanisole	1.5	1.0	3	76	4	3
3	**1c**	anisole	1.5	3.0	4	81 (85/15)	4	11
4	**1d**	*p*-methylanisole	1.5	3.0	3	71	3	6
5	**1e**	2,6-dimethylanisole	1.5	1.0	7	61	0	5
6	**1e**	anisole	1.5	1.0	10	73 (84/16)	0	3
7	**1e**	*p*-methylanisole	1.5	1.0	3	74	0	0
8	**1e**	2,6-dimethylanisole	1.5	1.0	5	65	0	1

[a] Reactions were performed using **1** (5.0 mmol) and 5 equiv of anisole in 30 mL of CCl_4. [b] The product distributions in all cases were determined by GLC with an internal standard. [c] Overall yield of mono- and dibrominated arene.

naphthalenes, did not react with *p*-benzoquinone methide; hence, 2,6-di-*tert*-butylbenzoquinone methide was dimerized very slowly. However, nuclear brominated products on arenes were eventually formed as well. Anisoles with moderately to non-activated substituents were readily hydroxybenzylated with *p*-benzoquinone methide.

We extended the intermolecular electrophilic substitution of anisoles with other symmetrical *p*-benzoquinone methides (Table 4). In all cases, *p*-hydroxybenzylated products **15** were obtained in reasonable yields. In general, the reaction was highly regioselective (>84%) to give the *para*-substituted products with anisole, and the regioselectivity was independent of the substituent on *p*-benzoquinone methide.

(3) Diels−Alder Reaction of *p*-Benzoquinone Methides. In a further effort to prove the formation of transient intermediate **3a** in the reaction of 2,6-di-*tert*-butyl-4-methylphenol with NBS in either DMSO or CCl_4, we trapped **3a** with 2,3-dimethylbutadiene to form spiroketone **17** (eq 10).[3] Spiroketones were first synthesized by treating **1a** with lead dioxide in the presence of diene, and this reaction proceeded via entrapment of a benzoquinone methide intermediate to give a [4 + 2] cycloadduct. Initially, we prepared spiroketone by treating 2,3-dimethylbutadiene with *p*-benzoquinone methide, which was completely formed in the mixture of **1a** and NBS in CCl_4, and obtained yields as high as 43%. Product identification by NMR was straightforward. Because the *p*-benzoquinone methide dienophile could be trapped, it followed that in situ formation of *p*-benzoquinone methide in the reaction of **1a** with NBS−DMSO in the presence of 2,3-dimethylbutadiene should give a direct synthesis of spiroketone. A mixture of **1a**, NBS, and 2,3-dimethylbutadiene in DMSO heated to 80 °C afforded spiroketone **17** in 53% yield. Our Diels−Alder cycloaddition reactions are promoted by Lewis acids. Thus, we next turned our attention to a variation of this reaction using Lewis acids, which proceeds with *p*-benzoquinone methide to provide the product in a higher yield. Among the Lewis acids tried, we found that the reaction using Et_2AlCl gave the best result. Table 5 shows the results of the direct [4 + 2] cycloaddition reaction of 2,6-di-*tert*-butyl-4-methylphenols with NBS−DMSO in the presence of Et_2AlCl. In all cases, hydroxybenzaldehyde was obtained in 5−15% yield.

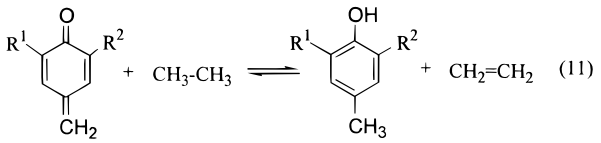


(10)

Table 5. [4 + 2] Cycloaddition Reaction of 2,6-Di-*tert*-butylbenzoquinone Methides 3a Directly Generated in Situ from 1a and NBS−DMSO

entry	diene	NBS (mmol)	Et_2AlCl (mmol)	time (h)	product (%)
1	2,3-dimethylbutadiene	1.5	1.5	5	64
2	isoprene	1.5	1.5	15	60
3	butadiene	2.5	2.5	7	67

(4) Electronic Considerations of *p*-Benzoquinone Methides. The in situ formation of benzoquinone methide by NBS was very sensitive to the electronic effect of the corresponding phenols. Thus, the stabilities of *p*-benzoquinone methides, **3a** (R^1, R^2 = *t*-Bu), **3e** (R^1, R^2 = Me), **3f** (R^1 = *t*-Bu, R^2 = H), and **3h** (R^1, R^2 = H) were calculated using density functional (DFT) geometry optimizations at the Becke 3-Lee−Yang−Parr (B3LYP) DFT level.[22] Density functional methods, and B3LYP in particular, can provide more reliable relative stabilization energies of intermediates than the Hartree−Fock calculation.[23] We compared the relative stabilities at the B3LYP/6-31G* level by means of isodesmic equations such as that illustrated in eq 11.



(11)

The stabilization energies for **3a**, **3e**, **3f**, and **3h** are +10.18, +7.65, +4.87, and +4.09 kcal/mol, respectively (Table 6). Even though one *tert*-butyl group in **3f** has a conjugation effect, the energy of **3f** is ∼3 kcal/mol lower than that of dimethylbenzoquinone methide **3e**. The higher stabilization energies for symmetrically hindered

(22) The density functional theory calculations employed Becke's three parameter hybrid method (Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652) and the correlation functional of Lee (Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, 785−789) within the Gaussian 94 program: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, w.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *GAUSSIAN 94*, Revision B.2; Gaussian, Inc.: Pittsburgh, PA, 1995.

(23) (a) Freeman, P. K. *J. Am. Chem. Soc.* **1998**, *120*, 1619. (b) Patterson, E. V.; McMahon, R. J. *J. Org. Chem.* **1997**, *62*, 4398. (c) Ammann, J. R.; Subramanian, R.; Sheridan, R. S. *J. Am. Chem. Soc.* **1992**, *114*, 7592. (d) Liu, J.; Niwayama, S.; You, Y.; Houk, K. N. *J. Org. Chem.* **1998**, *63*, 1064. (e) Halton, B.; Cooney, M. J.; Boese, R.; Maulitz, A. H. *J. Org. Chem.* **1998**, *63*, 1583.

Table 6. Stabilization Energies of *p*-Benzoquinone Methides Calculated at the B3LYP/6-31G*//B3LYP/6-31G* Level[a]

3 (R^1, R^2)	BM	ethane	phenol	ethene	SE[b] (kcal/mol)
3a, (*t*-Bu, *t*-Bu)	−660.052585	−79.830417	−661.279322	−78.587456	+10.18
3e, (Me, Me)	−424.020497	−79.830417	−425.413180	−78.587456	+7.65
3f, (*t*-Bu, H)	−502.796942	−79.830417	−504.032136	−78.587456	+4.87
3h, (H, H)	−345.432362	−79.830417	−346.776027	−78.587456	+4.09

[a] Energies in hartrees were uncorrected for zero-point energy. [b] The stabilization energy SE = $E_{phenol} + E_{ethene} - E_{BM} - E_{ethane}$ in kcal/mol.

benzoquinone methides **3a** and **3e**, compared to **3f** and **3h**, can explain the conjugation effects. In particular, di-*tert*-butylbenzoquinone methide **3a** displays a symmetrically bisected geometry without distortion, and thus it gives an unusually higher stabilization energy. The relatively high stabilization energies for **3a** and **3e** are consistent with the experimental results that the formation of *p*-benzoquinone methide with NBS is predominant.

Summary

We examined the NBS oxidation of symmetrically hindered alkylphenols to afford a *p*-benzoquinone methide **3** under mild conditions. Trapping of the electrophilic exocyclic alkylidene in **3** by DMSO provides an efficient route to formylphenols. This oxidation reaction is strongly activated by the generation of more electrophilic methine by the addition of bromodimethylsulfonium bromide to **3**. Strikingly, the side-chain halogenation reaction of symmetrically hindered alkylphenols does not occur with NBS under free-radical conditions. However, when unsymmetrically hindered methylphenols or *p*-cresol were allowed to react with NBS in DMSO, the nuclear bromination process was predominant. Some attempts were made to take advantage of the electrophilic and double bond characters of benzoquinone methide that would indicate its intermediacy in the NBS-promoted reaction. First, the electrophilic substitution reaction of moderately activated anisoles provided *p*-hydroxybenzylated anisoles in good yields. Second, the [4 + 2] cycloaddition reaction with diene also proceeded to give reasonable yields. In addition, the ab initio calculations show that the relative stabilization energies of the symmetrically hindered benzoquinone methides account for their stability.

Experimental Section

^{1}H NMR spectra were recorded on a 300 MHz spectrometer in $CDCl_3$ solution. Mass spectra were obtained at a 70 eV via GC−MS coupling. GC analyses were performed using a capillary column (25 m × 0.2 mm i.d.). Melting points were determined on a Mel-Temp II apparatus and were uncorrected. 3,5-Di-*tert*-butyl-4-hydroxybenzyl bromide[3b] was prepared from 3,5-di-*tert*-butyl-4-hydroxybenzyl alcohol and HBr gas according to the published procedure. The known products (**2a**−**e**, **11**, **and 16**) were identical in all respects (mp, IR, MS, and NMR) with those previously reported.

General Procedure for the Oxidation of 2,6-Di-*tert*-butyl-4-methylphenol. NBS (0.213 g, 1.2 mmol) was added to a solution of 2,6-di-*tert*-butyl-4-methylphenol (0.220 g, 1.0 mmol) in DMSO (10 mL). The reaction mixture was heated at 120 °C for the time given in Table 2. After the reaction was completed, brine solution and methylene chloride were poured into the flask. The separated organic layer was washed with water and dried over magnesium sulfate. The solvent was removed in vacuo, and the residue was chromatographed with hexanes−ethyl acetate (9:1) to give the product.

3,5-Di-*tert*-butyl-4-hydroxybenzaldehyde (2a): mp 179−181 °C (lit.[24a] 178−181 °C); ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 18H), 5.77 (s, 1H), 7.66 (s, 2H), 9.79 (s, 1H); LRMS (EI) *m*/*z* 234 (M^+).

3,5-Dimethoxy-4-hydroxybenzaldehyde (Syringaldehyde) (2b): mp 110−111 °C (lit.[24b] 111−112 °C); ^{1}H NMR ($CDCl_3$) δ 3.89 (s, 6H), 6.16 (s, 1H), 7.19 (s, 2H), 10.18 (s, 1H); LRMS (EI) *m*/*z* 182 (M^+).

3,5-Diphenyl-4-hydroxybenzaldehyde (2c): mp 167−168 °C (lit.[24c] 168−170 °C); ^{1}H NMR ($CDCl_3$) δ 5.96 (s, 1H), 7.40−7.55 (m, 10H), 7.81 (s, 2H), 9.94 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 128.4, 129.1, 129.2, 129.5, 129.9, 131.8, 136.1, 154.8, 190.9; LRMS (EI) *m*/*z* 274 (M^+).

3,5-Diisopropyl-4-hydroxybenzaldehyde (2d): mp 103−105 °C (lit.[24d] 106−108 °C); ^{1}H NMR ($CDCl_3$) δ 1.30 (d, J = 6.7 Hz, 12 H), 3.23 (m, 2H), 6.14 (s, 1H), 7.64 (s, 2H), 9.85 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 22.50, 26.96, 126.26, 129.46, 134.56, 156.26, 192. 01; LRMS (EI) *m*/*z* 206 (M^+).

3,5-Dimethyl-4-hydroxybenzaldehyde (2e): mp 111−113 °C (lit.[24e] 111−112 °C); ^{1}H NMR ($CDCl_3$) δ 2.24 (s, 6H), 5.68 (s, 1H), 7.47 (s, 2H), 9.73 (s, 1H); LRMS (EI) *m*/*z* 150 (M^+).

3,5-Di-*tert*-butyl-2-hydroxybenzaldehyde (13): mp 54−57 °C (lit.[16] 53−56 °C); ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 9H), 1.34 (s, 9H), 7.27 (s, 1H), 7.51 (s, 1H), 9.79 (s, 1H), 11.66 (s, 1H); LRMS (EI) *m*/*z* 234 (M + 1).

General Procedure for the Arylation with 2,6-Di-*tert*-butyl-4-methylphenol. NBS (1.331 g, 7.5 mmol) was added to a mixture of 2,6-di-*tert*-butyl-4-methylphenol (1.101 g, 5 mmol), anisole (2.717 mL, 25 mmol), and $ZnCl_2$ (0.681 g, 5 mmol) in CCl_4 (30 mL). The reaction mixture was heated at 120 °C for the time given in Table 4. After the reaction was completed, brine solution and methylene chloride were poured into the flask. The separated organic layer was washed with water and dried over magnesium sulfate. The solvent was removed in vacuo, and the residue was chromatographed with hexanes−ethyl acetate (9:1) to give the product **15**.

2,6-Di-*tert*-butyl-4-[(4′-methoxyphenyl)methyl]phenol (*para* product):[9] mp 136−137 °C; ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 18H), 3.70 (s, 3H), 3.73 (s, 2H), 4.97 (s, 1H), 6.75 (d, J = 8.5 Hz, 2H), 6.90 (s, 2H), 7.04 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 30.6, 34.6, 41.2, 55.5, 114.0, 125.6, 130.0, 132.3, 134.2, 136.1, 152.2, 158.1 ppm; LRMS (EI) *m*/*z* 326 (M^+); HRMS calcd for $C_{22}H_{30}O_2$ 326.2246, found 326.2237.

2,6-Di-*tert*-butyl-4-[(2′-methoxy-5′methylphenyl)methyl]phenol:[9] oil; ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 18H), 3.80 (s, 2H), 4.59 (s, 1H), 5.02 (s, 1H), 6.65 (m, 1H), 6.85 (m, 2H), 6.98 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 19.5, 29.3, 33.3, 35.5, 114.6, 124.1, 126.0, 127.0, 128.9, 130.4, 135.2, 150.7, 151.4; MS (EI) 326 (M^+); HRMS calcd for $C_{22}H_{30}O_2$ 326.2246, found 326.2246.

2,6-Di-*tert*-Butyl-4-[(4′-methoxy-3′,5′-dimethylphenyl)-methyl]phenol: mp 92−94 °C; ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 18H), 2.16 (s, 6H), 3.60 (s, 3H), 3.69 (s, 2H), 4.97 (s, 1H), 6.76 (s, 2H), 6.91 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 16.1, 30.3, 34.3, 41.2, 59.6, 125.3, 129.1, 130.5, 131.8, 135.7, 137.0, 152.0, 155.1; LRMS (EI) *m*/*z* 354 (M^+); HRMS calcd for $C_{24}H_{34}O_2$ 354.2558, found 354.2550.

2,6-Diisopropyl-4-[(4′-methoxyphenyl)methyl]phenol (*para* product): oil; ^{1}H NMR ($CDCl_3$) δ 1.25 (d, J = 6.96 Hz,

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12H), 3.14 (m, 2H), 3.80 (s, 3H), 3.85 (s, 2H), 4.71 (s, 1H), 6.84−6.88 (m, 4H), 7.18 (d, J = 8.43 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 22.71, 27.19, 40.67, 55.20, 113.70, 123.85, 129.61, 133.17, 133.54, 133.94, 148.14, 157.70; LRMS (EI) m/z 298 (M^+); HRMS calcd for $C_{20}H_{26}O_2$ 298.1933, found 298.1922.

2,6-Diisopropyl-4-[(2′-methoxy-5′methylphenyl)methyl]phenol: oil; ^{1}H NMR ($CDCl_3$) δ 1.27 (d, J = 6.75 Hz, 12H), 2.25 (s, 3H), 3.15 (m, 2H), 3.83 (s, 3H), 3.89 (s, 2H), 4.67 (s, 1H), 6.78 (d, J = 8.04 Hz, 2H), 6.89 (s, 1H), 6.97 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 20.56, 22.80, 27.24, 35.58, 55.46, 110.28, 124.15, 127.30, 129.59, 130.20, 130.81, 132.71, 133.34, 148.04, 155.23; LRMS (EI) m/z 312 (M^+); HRMS calcd for $C_{21}H_{28}O_2$ 312.2089, found 312.2072.

2,6-Diisopropyl-4-[(4′-methoxy-3′,5′-dimethylphenyl)-methyl]phenol: mp 100−102 °C; ^{1}H NMR ($CDCl_3$) δ 1.23 (d, J = 6.96 Hz, 12H), 2.23 (s, 6H), 3.12 (m, 2H), 3.68 (s, 3H), 3.78 (s, 2H), 4.70 (s, 1H), 6.82 (s, 2H), 6.87 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 16.1, 22.7, 27.2, 41.0, 59.7, 123.9, 129.0, 130.5, 133.0, 133.6, 137.1, 148.2, 155.0; LRMS (EI) m/z 326 (M^+); HRMS calcd for $C_{22}H_{28}O_2$ 324.2089, found 324.2089.

2,6-Dimethyl-4-[(4′-methoxyphenyl)methyl]phenol(*para* product): oil; ^{1}H NMR ($CDCl_3$) δ 2.17 (s, 6H), 3.75 (s, 3H), 3.80 (s, 2H), 4.53 (s, 1H), 6.76∼6.82 (m, 4H), 7.14 (d, J = 29.28 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 15.85, 40.13, 55.18, 113.77, 122.94, 128.85, 129.63, 133.12, 133.93, 150.36, 157.76; LRMS (EI) m/z 242 (M^+); HRMS calcd for $C_{16}H_{18}O_2$ 242.1307 found 242.1303.

2,6-Dimethyl-4-[(2′-methoxy-5′-methylphenyl)methyl]-phenol: mp 50∼52 °C; ^{1}H NMR ($CDCl_3$) δ 2.04 (s, 6H), 2.20 (s, 3H), 3.74 (s, 3H), 3.78 (s, 2H), 4.52 (s, 1H), 6.69∼6.94 (m, 5H);^{13}C NMR ($CDCl_3$) δ 15.79, 20.40, 34.69, 55.43, 110.41, 122.78, 127.33, 128.92, 129.49, 129.92, 130.88, 132.57, 150.15, 155.10; MS (from GC−MS) 256 (M^+); HRMS calcd for $C_{17}H_{20}O_2$ 256.1463, found 256.1453.

2,6-Dimethyl-4-[(4′-methoxy-3′,5′-dimethylphenyl)-methyl]phenol: mp 82−83 °C; ^{1}H NMR ($CDCl_3$) δ 2.18 (s, 6H), 2.22 (s, 6H), 3.74 (s, 3H), 3.69 (s, 3H), 6.78−6.80 (d, J = 5.07 Hz, 2H);^{13}C NMR ($CDCl_3$) δ 15.86, 40.44, 59.59, 122.98, 128.88, 128.97, 130.51, 132.94, 137.04, 150.40, 155.00; LRMS (EI) m/z 281 ($M - 1^+$); HRMS calcd for $C_{18}H_{22}O_2$ 270.1631, found 270.1619.

Diels−Alder Reaction of 2,6-Di-*tert*-butyl-4-methylphenol with Dienes. To a mixture of 2,6-di-*tert*-butyl-4-methylphenol (0.220 g, 1.0 mmol) and $ZnCl_2$ (0.408 g, 3 mmol) in DMSO (10 mL) equipped with an ice-cooled condenser was added NBS (0.266 g, 1.5 mmol). Diene (1 mL) was introduced; the resulting mixture was refluxed for 3 h. After the mixture cooled, water and methylene chloride were added. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed in vacuo, and the residue was chromatographed to give the product **17**.

2,4-Di-*tert*-butyl-8-methyl-spiro[5.5]undeca-1,4,7-trien-3-one: mp 73−75 °C (lit.[3b] 73−74 °C); ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 18H), 1.60 (t, J = 6.4 Hz, 2H), 1.75 (s, 3H), 2.00−2.14 (m, 4H), 5.43 (t, J = 1.6 Hz, 1H), 6.60 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 23.3, 27.8, 29.5, 33.7, 34.6, 35.1, 37.1, 118.3, 133.2, 145.7, 185.7, 186.7; LRMS (EI) m/z 286 (M^+).

2,4-Di-*tert*-butyl-7,8-dimethyl-spiro[5.5]undeca-1,4,7-trien-3-one: ^{1}H NMR ($CDCl_3$) δ 1.19 (s, 18H), 1.48 (t, J = 6.5 Hz, 2H), 1.57 (d, J = 1.6 Hz, 3H), 1.63 (d, J = 0.6 Hz, 3H), 1.87 (s, 2H), 2.00 (brs, 2H), 6.53 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 17.8, 18.1, 28.3, 28.5, 32.8, 33.6, 37.2, 40.1, 121.8, 123.7, 144.9,-185.0, 185.7; LRMS (EI) m/z 300 (M^+).

2,4-Di-*tert*-butylspiro[5.5]undeca-1,4,7-trien-3-one: ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 18H), 1.60 (t, J = 3.2 Hz, 2H), 2.02−2.19 (brm, 4H), 5.71−5.87 (brm, 2H), 6.63 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 23.3, 29.9, 33.4, 35.0, 35.2, 37.5, 124.6, 126.7; LRMS (EI) m/z 272 (M^+).

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