26750). Use of the high-field NMR spectrometer used in these studies was made possible through equipment grants from the NIH and NSF.

Registry No. 1, 2525-55-5; 3, 137091-70-4; 4, 137059-18-8; 5, 137059-19-9; 6, 137091-71-5; 7, 15515-75-0; 8, 137059-20-2; 9, 137059-21-3; 10, 137059-22-4; 11, 137059-23-5; 12, 137059-24-6; 13, 137059-25-7; 14, 137059-26-8; 15, 137059-27-9; 16, 137059-28-0; 17, 137059-29-1; 18, 137059-30-4; 19, 137059-31-5; 20, 137059-32-6; 21, 137059-33-7; 22, 137059-34-8; 23, 112841-18-6; 25, 137059-35-9; 26, 34259-63-7; 28, 137059-36-0; 29, 137059-37-1; 30, 137059-38-2; 32, 137059-39-3; 33, 129855-21-6; 34, 129855-24-9; 35, 129855-25-0; 36, 137059-40-6; 37, 129855-23-8; 38, 6947-57-5; 39, 129855-22-7; 40, 137059-41-7; $PhNH_2$, 62-53-3; $PhCH_2NH_2$, 100-46-9; *t*-$BuNH_2$, 75-64-9; $MeNH_2$, 74-89-5; $PhCH_2NH(CH_2)_2OH$, 104-63-2; PhSH, 108-98-5; *t*-BuCOCl, 3282-30-2; $Br(CH_3)C{=}CHCH_3$, 13294-71-8; $ClCO(CH_2)_3Br$, 927-58-2; BrC_6H_4-*o*-CH_2Br, 3433-80-5; $Br(CH_2)_3Br$, 109-64-8; 3-(phenylsulfonyl)-2-(phenylthio)-1-propene, 2525-54-4; 2-piperidinemethanol, 3433-37-2; *N*-[2-(phenylsulfonyl)-2-propenyl]-2-piperidinemethanol, 137059-42-8; 2-(bromomethyl)-*N*-[2-(phenylsulfonyl)-2-propenyl]piperidine, 137059-43-9; furfurylamine, 617-89-0; dibenzylethylenediamine, 140-28-3; ethanedithiol, 540-63-6; bis(phenylsulfonyl)methane, 3406-02-8; 2,4-pentanedione, 626-96-0; 1-pyrrolidino-1-cyclohexene, 1125-99-1; 3-(phenylsulfonyl)bicyclo[3.3.1]nonan-9-one oxime, 137059-36-0; sodium pyrithione, 15922-78-8; cyclopentaneacetyl chloride, 1122-99-2; cyclohexanecarbonyl chloride, 2719-27-9; cyclohexyl bromide, 108-85-0.

Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra (75 MHz) for all compounds with high resolution mass spectra (13 pages). Ordering information is given on any current masthead page.

Reinvestigation on the Reaction of 2,6-Di-*tert*-butylbenzoquinone Methide and 2,6-Di-*tert*-butylphenol

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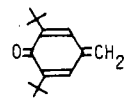
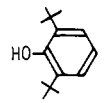
The reaction of quinone methide 1 and phenol 2 in equimolar amounts was investigated in pentane at 30 °C. Products were isolated by means of column chromatography on SiO_2. There was a marked difference in product distribution between the reactions in the presence and absence of added Et_3N. Dienones 3 and 10 were obtained only from the former reaction, while formation of 1,2-bis(4-hydroxyphenyl)ethane 18 and 4,4'-dihydroxybiphenyl 20 was overwhelming in the latter reaction. Other products from both reactions were relatively small quantities of 4,4'-stilbenequinone 17, 4,4'-diphenoquinone 21, and bis(4-hydroxyphenyl)methane 24, but dienone 4 was not obtained. Compounds 20 and 24 obtained from the latter reaction were formed by isomerization of dienones 19 and 23, respectively, during the chromatography. The reaction is initiated by dimerization of 1 to generate biradical 11. Subsequent processes involving hydrogenation–dehydrogenation, coupling–dissociation, and dienone–phenol rearrangement account for the formation or the lack of formation of the products. The difference in product distribution is ascribed to capability of Et_3N to catalyze the isomerization. Quinone methide 1 also adds to 2 to give 23. The decay of 1 in the presence of both 2 and phenol 6 gave dienone 8 additionally. The formation of 24 and 4 was facilitated by conducting the reaction of 1 and 2 in DMSO. Dehydrogenation of 10 and 3 with PbO_2 afforded spirodienones 27 and 28, respectively. Compounds 27 and 28 were unstable, and their decay in solution was investigated in the presence or absence of added 2. The results show that the decay is initiated by homolytic scission of the C–C bond connecting the dienone rings in the cyclopentane (in 27) and cyclohexane (in 28) rings. Compound 28 is novel in that it bears two kinds of such C–C bonds. Reversibility of the dimerization of 1 is suggested.

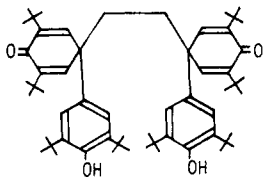
2,6-Di-*tert*-butylbenzoquinone methide (1) is a reactive species which can exist only in dilute solution, and its reactions have been investigated in considerable detail, partly in connection with the antioxidant activity of 2,6-di-*tert*-butyl-4-methylphenol (6).[1] Neureiter[2] studied the decay of 1 in the presence of 2,6-di-*tert*-butylphenol (2) in petroleum ether under various conditions and obtained bis-dienone 3 in generally low yields. Later, Chaser and Westfahl[3] conducted a similar reaction, but in the presence of base such as dimsyl anion or Et_3N, and isolated dienone 4.



1



2



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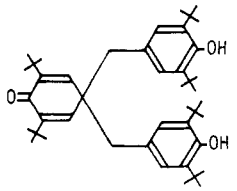


4

Recently, it has been suggested by a ^1H NMR study that addition of 2 to a solution containing 1 generated by disproportionation of phenoxy radical 5 slowly affords, in the presence of a base, dienone 8 among other products.[4] This

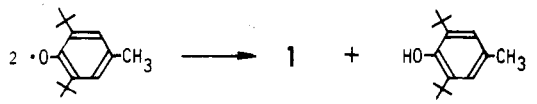
(1) (a) Forrester, A. R.; Hay, J. M.; Thomson, R. H. In *Organic Chemistry of Stable Free Radicals*; Academic Press: New York, 1968; p 281. (b) Volod'kin, A. A.; Ershov, V. V.; Kudinova, L. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1978**, 512. (c) Kudinova, L. I.; Volod'kin, A. A.; Ershov, V. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1978**, 1661. (d) Becker, H.-D.; Sanchez, D. *Tetrahedron Lett.* **1975**, 3745. (e) Roper, J. M.; Everly, C. R. *J. Org. Chem.* **1988**, *53*, 2639. (f) McClure, J. D. *J. Org. Chem.* **1962**, *27*, 2365. (g) Woolhouse, A. D. *Aust. J. Chem.* **1977**, *30*, 1145. (h) Bruk, Yu A.; Rachinskii, F. Yu *Zh. Obsch. Khim.* **1964**, *34*, 2983. (i) Schmidt, A.; Brunetti, H. *Helv. Chim. Acta* **1976**, *59*, 522. (j) Starnes, Jr., W. H.; Myers, J. A.; Lauff, J. J. *J. Org. Chem.* **1969**, *34*, 3404. (k) Starnes, Jr., W. H.; Lauff, J. J. *J. Org. Chem.* **1970**, *35*, 1978. (l) Goulart, M. O. F.; Utley, J. H. P. *J. Org. Chem.* **1988**, *53*, 2520.

(2) Neureiter, N. P. *J. Org. Chem.* **1963**, *28*, 3486.

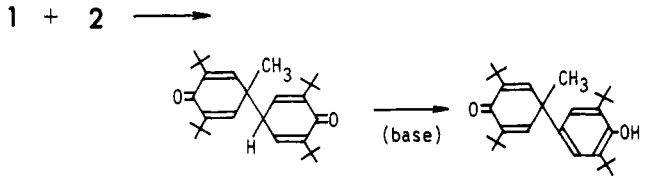
(3) Chaser, D. W.; Westfahl, J. C. *J. Org. Chem.* **1977**, *42*, 2177.

0022-3263/92/1957-0306$03.00/0

suggested a possibility that 8 was the product of addition of 2 to 1. The author reinvestigated carefully the reaction



5 6

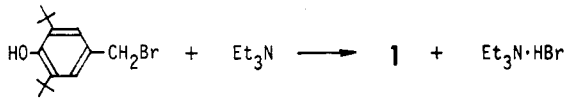


7 8

of 1, generated by a method similar to those employed by Neureiter and by Chaser and Westfahl, and 2 in the presence or absence of Et_3N. The outcome of such a study was more than originally expected, and it is reported in this paper.

Results and Discussion

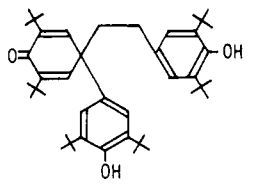
A dilute solution of 1 prepared by treatment of benzyl bromide 9 in pentane with exactly 1 mol equiv or slightly less than 1 mol equiv of Et_3N and subsequent filtration to remove Et_3N·HBr, was added to a solution of 2 (1 mol equiv) in pentane containing or not containing excess Et_3N.



9

The mixture was concentrated to a small volume, let stand at 30 °C for 20 h, and evaporated to leave a residue, which was subjected to column chromatography on SiO_2 for product analysis (Table I). No 8 was isolated from the reaction in the presence (run 2) or absence (run 1) of Et_3N. The addition of 2 to 1 to form 8 via bis-dienone 7 is, therefore, unlikely to be operative.

There was a remarkable difference in product distribution between the reactions in the presence and absence of added Et_3N. Bis-dienone 3 was obtained only from run 2 in low yield. A most remarkable feature was formation of a new compound as the major product from run 2 and its lack of formation from run 1. Elemental analysis suggested that the nearly colorless product, mp 164.5–166.5 °C dec, was isomeric with 4. Phenolic dienone structure 10 was consistent with the ^1H NMR spectrum ($CDCl_3$),



10

which exhibited singlets at δ 7.09 (2 H), 6.96 (2 H), 6.60 (2 H), 5.14 (1 H), 5.06 (1 H), 2.39 (4 H), 1.44 (18 H), 1.42 (18 H), and 1.27 (18 H). The signals due to protons of the nonequivalent methylene groups are assumed to be superimposed at δ 2.39. The ^{13}C NMR spectrum showed

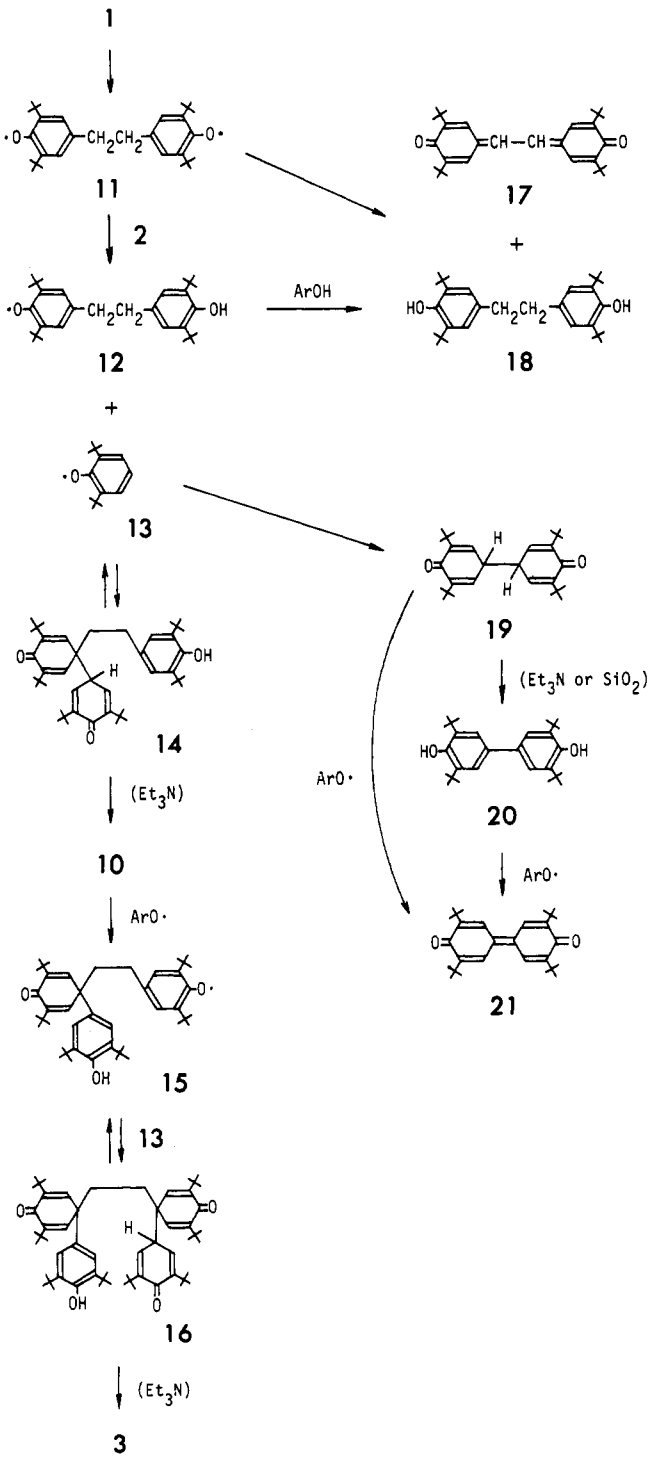
(4) Omura, K. *J. Org. Chem.* **1991**, *56*, 921.

Table I. Reaction of Quinone Methide 1 and Phenol 2[a]

run	additive	recovery of 2 (%)	products[b] (%[c])						
			3	10	17	18	20	21	24
1	none	23	0	0	4	66	59	4	6
2	Et_3N	43	9	53	0	34	1	13	0.4

[a] In pentane using equimolar amounts of 1 and 2. [b] Isolated by column chromatography on SiO_2. [c] For 24, (mol/mol 1 or 2 employed) × 100; for the other products (mol/mol 1 or 2 employed) × 2 × 100.

Scheme I

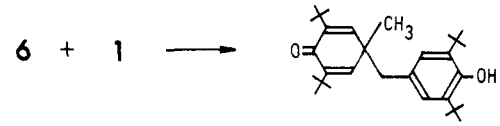


signals at δ 39.32 and 30.88 attributable to methylene carbons. The formation or the lack of formation of 10 and 3 may be explained in the following manner (Scheme I). The reaction is initiated by dimerization of 1 to give bi-

radical 11. The radical has been suggested to disproportionate to give 1,2-bis(4-hydroxyphenyl)ethane 18 and 4,4′-stilbenequinone 17.[1a,5] In the presence of 2, 11 is partially hydrogenated to generate monoradical 12 while 2 is dehydrogenated to give phenoxy radical 13. Coupling of 12 and 13 provides bis-dienone 14. Intermediate 14 is unstable and is either reverted to 12 and 13 by dissociation or converted into 10 by spontaneous isomerization. The latter process is slow at 30 °C but is catalyzed by Et_3N. Such reactivity of 14 is analogous to that of 7; 7 tends to reversibly dissociate to give 5 and 13 but is isomerized into 8 if Et_3N is present.[4] Dehydrogenation of 10 with phenoxy radicals such as 13 in the solution (ArO• in Scheme I) followed by coupling of the resulting phenoxy radical 15 with 13 provides tris-dienone 16, which is as unstable as 14. In the absence of added Et_3N, the net consumption of phenoxy radicals 12 and 13 generated by the reaction of 11 with 2, therefore, is principally brought about not by their coupling to give 14 but by hydrogenation with phenols such as more 2 in the solution (ArOH) to give 18 and by dimerization to afford bis-dienone 19, respectively.[6] Indeed, formation of 18 and 4,4′-dihydroxybiphenyl 20 from run 1 was substantial while they were obtained in much lower yields from run 2. Compound 20 obtained from run 1 was probably produced by isomerization of product 19 during the chromatography, since the ^1H NMR spectrum ($CDCl_3$) of the crude product (before chromatography) indicated that it contained little 20 but a substantial quantity of 19 (presence of a doublet at δ 6.46 and a triplet at δ 3.40[4]). Upon addition of pyridine-d_5, these signals rapidly disappeared from the spectrum and a new singlet at δ 7.23 ascribable to 20 appeared. Relative stability of 19 in a nonpolar solvent at 30 °C and its facile transformation into 20 by SiO_2 or base have been reported.[4] A high 20/4,4′-diphenoquinone 21 ratio from run 1 and the low ratio from run 2 are also notable, although the total yield of 20 and 21 from run 1 was much higher than that from run 2. The relatively small quantity of 21 obtained from run 1 may have been produced by inefficient dehydrogenation of 19 with ArO• and/or by the efficient dehydrogenation of 20 formed from 19 by slow and spontaneous isomerization.

Neureiter[2] observed that the formation of 3 from the reaction of 1 and 2 (in the absence of base) was favored at low temperature (−15 °C) and that no 3 was obtained if the reaction was conducted at 45 °C. This may suggest that the rates of dissociation of 14 and 16 are more sensitive to temperature than those of their competitive spontaneous dienone–phenol isomerization. Hence, the isomerization of 14 (to give 10) and 16 (to give 3) becomes more significant at lower temperature, but their dissociation overwhelms at high temperature. As described below, however, the reaction of 15 with 13 (in the absence of Et_3N) at 60 °C did afford a small quantity of 3, if they were simultaneously generated by a different means without intervention of 14 or 10. This suggests that a small fraction of 16 derived from 15 and 13 underwent the spontaneous isomerization even at 60 °C. The lack of formation of 3 from the reaction of 1 and 2 above 30 °C, therefore, is attributable to the lack of formation of 10 in a sufficient quantity from which 15 can be derived.

By examining the ^1H NMR spectrum of the crude product, Neureiter[2] concluded that it did not contain bis(4-hydroxyphenyl)methane 24, a possible product from the reaction between 1 and 2. A survey of the ^1H NMR spectrum ($CDCl_3$) of the crude product from run 1 led to the same conclusion. Upon addition of pyridine-d_5, however, a new small singlet at δ 3.80 ascribable to 24 appeared in the spectrum. After the chromatography, 24 was isolated in low yield. Accordingly, it is reasonably assumed that 2 adds to 1 (in the absence of base) to afford dienone 23 (but not 7) and that 23 is relatively stable in pentane at 30 °C but is easily transformed into isomer 24 by base or SiO_2. Chaser and Westfahl,[3] having observed the formation of 24 as well as 4 from the reaction of 1 and 2 in the presence of bases, considered that the role of the bases was to convert 2 (and presumably 24 too) into the corresponding phenolate anion, which was the real species that added to 1 to afford 24 (and 4). From run 2, only a trace amount of 24 was obtained while 4 was not obtained at all.[7] The only role of Et_3N in the reaction of 1 and 2 to form 24 in run 2 appears to be in isomerizing intermediate 23, and a small amount of 24 formed was perhaps consumed principally by other reactions such as dehydrogenation (see below) than addition to 1 to give 4. For the account of the obtainment by Chaser and Westfahl of 4 albeit in apparently low yield, a recent finding in this laboratory was suggestive that addition of 6 to 1 to give dienone 22 is promoted in polar solvents such as DMSO but not by Et_3N.[8]

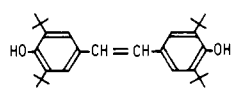


22

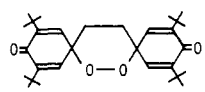
By analogy, the additions of 2 and 24 to 1 giving rise to 23 and 4, respectively, were assumed to be facilitated by DMSO, the solvent employed in the study of the original authors. Since 19 was found to be facilely transformed into isomer 20 in DMSO-d_6 as shown by a ^1H NMR study, it seemed also reasonable to assume that isomerization of 23 into 24 was similarly facile in DMSO. The reaction of 1 and 2 in DMSO (in the absence of Et_3N) was undertaken and found to yield 24 and 4 in 7 and 8% yields, respectively, along with the other products obtained from run 2 (Table I). The reaction of 1 and 24 in DMSO gave 4 in 55% yield (or 77% yield based on the reacted 24). The yield was not improved by addition of Et_3N. The same reaction conducted in pentane containing Et_3N afforded 4 only in 11% yield, and formation of dienone 25, the product of dehydrogenation of 24, was significant (31%). In conclusion, the overall process of the formation of 4 from 1 and 2 is facilitated by DMSO rather than by base (Scheme II).

As described above, the reactions of 1 and 2 did not afford 8. In the reported reaction to form 8, 1 was gen-

(5) The decay of 1 (in the absence of 2 or other additives) was also reinvestigated in this laboratory. The decay in pentane afforded only 0.08 and 0.05 equiv of 17 and 18, respectively, per 1 equiv of 1 employed. Formation of at least two other unidentified products was significant, none of which coincided with 4,4′-dihydroxystilbene i or peroxide ii (unpublished work). The result suggests that there is an additional reaction(s) by which 1 or (and) 11 can degrade spontaneously. These unidentified products were more or less formed in the reactions involving 1 which were carried out in inert solvents in the present study.



I



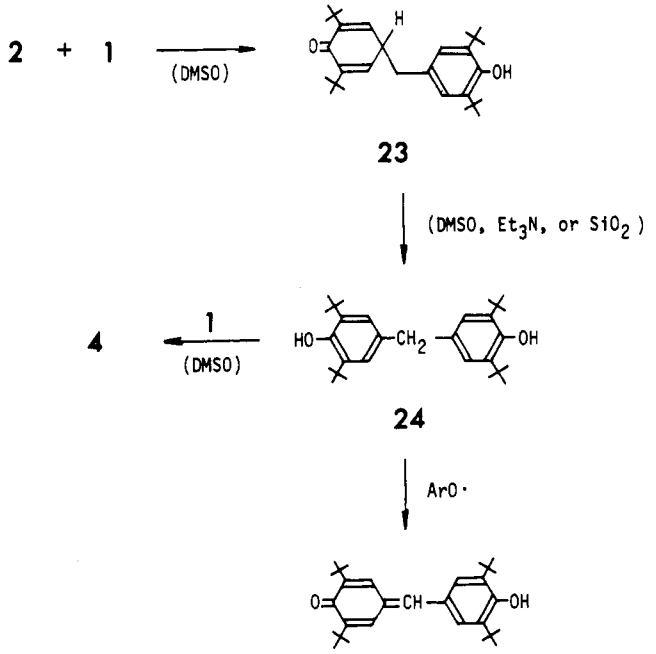
II

(6) In addition, 12 can be dehydrogenated by 13 to regenerate 11 and 2 (not shown in the scheme).

(7) Compound 4 was not obtained from run 1 either.

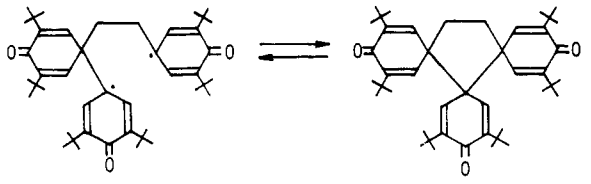
(8) The results will be published elsewhere.

Scheme II



erated by the disproportionation of **5**, which produced **6** simultaneously.[4] The reaction of **1** in the presence of both **2** (1 mol equiv) and **6** (1 mol equiv) carried out in an analogous manner to that described for run 2, gave **8** in 37% yield as well as the products obtained from run 2 (Table I). Little **8** (0.8%) was obtained if the addition of Et_3N was omitted. Accordingly, the formation of **8** will be interpreted as the result of generation of radicals **13** and **5** from **2** and **6**, respectively, by dehydrogenation with biradical **11**, and their subsequent coupling to form **7**.[4]

A number of spirocyclic compounds have been synthesized by intramolecular C–O coupling of biradicals generated from biphenolic compounds, although those obtained by the C–C coupling are relatively few.[9] Dehydrogenation of some of the biphenolic products obtained in this study was attempted. Exposure of **10** to PbO_2 in CH_2Cl_2 at ice-bath temperature afforded a nearly colorless compound, mp 160–161 °C dec, in 64% yield, which was determined to be terspiro-dienone **27** based on analytical and spectral data (see Experimental Section). Compound **27**, formed by cyclization of biradical **26**, was not very



26 **27**

stable. At 60 °C in hexane, **27** was degraded into products including **17** and **21**, although more than 50% of the **27** remained unchanged after 75 h. These products were probably formed by way of **26** generated by the reverse cyclization. The decay of **27** in the presence of **2** was completed faster (Table II). The reaction with excess **2** (5 mol equiv) gave **10** in nearly quantitative yield (run 1). A small quantity of **3** was also found. A similar reaction

(9) Musso, H. In *Oxidative Coupling of Phenols*; Taylor, W. I., Battersby, A. R., Eds.; Marcell Dekker: New York, 1967; p 1.

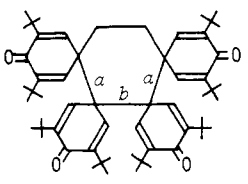
Table II. Decay of Spirodienone 27[a]

run	solvent	phenol 2 (mol equiv)	recovery of 2 (%)	products[b] (%[c]) 3	10	17	18	20	21
1	hexane	5	69	<2	99	NE[d]	0	35	34
2	hexane	1	4	6	88	NE[d]	NE[d]	<1	46
3	Et_3N	5	64	11	87	0	0	31	20
4	Et_3N	1	0	33	48	0	0	0.4	26
5	Et_3N	0		0	50	NE[d]	NE[d]	2	25
6	Et_3N/hexane	1	2	44	53	NE[d]	NE[d]	0	26

[a] At 60 °C for 16, 48, 15, 39, 65, and 26 h for runs 1, 2, 3, 4, 5, and 6, respectively. The decay of **27** was complete within these reaction times. [b] Isolated by column chromatography on SiO_2. [c] For all the products, (mol/mol **27** employed) × 100. [d] Not examined. Formed in a small quantity if at all.

conducted with an equimolar amount of **2** afforded more **3** than run 1 did, although the formation of **10** was still substantial (run 2). Thus, coupling of **15** with **13** (to give **16**), which are generated by reaction of **26** with **2**, competes more favorably with hydrogenation of **15** by more **2** (to give **10**) when less **2** is employed initially (confer Scheme I). The remarkably high yields of **10** (88%) and **21** (0.46 mol/mol **27** or **2** employed, or 91% assuming that all of the **21** was derived from **2**) obtained from run 2, indicate that hydrogens to reduce **27** were supplied not only by **2** but also by other hydrogen donors, **20** and/or **19**. It is possible that **19** was the principal donor, since the spontaneous isomerization (or dissociation) of **19** in CCl_4 was reluctant even at 60 °C; **19** was recovered largely unchanged after reaction for 50 h as suggested by ^1H NMR spectroscopy. As anticipated, the yield of **3** from runs 1 or 2 was improved by replacing the reaction solvent by Et_3N which, as described above, promotes the isomerization of **16** into **3** (runs 3 and 4). The thermal decomposition of **27** in Et_3N was found to afford, in addition to **21**, **10** even without added **2** by a relatively inefficient process (run 5). Biradical **26**, therefore, is reduced slowly by Et_3N. Hence the highest yield of **3** (44%) was furnished when **27** was allowed to disintegrate in the presence of **2** (1 mol equiv) in hexane containing a small amount of Et_3N (run 6).

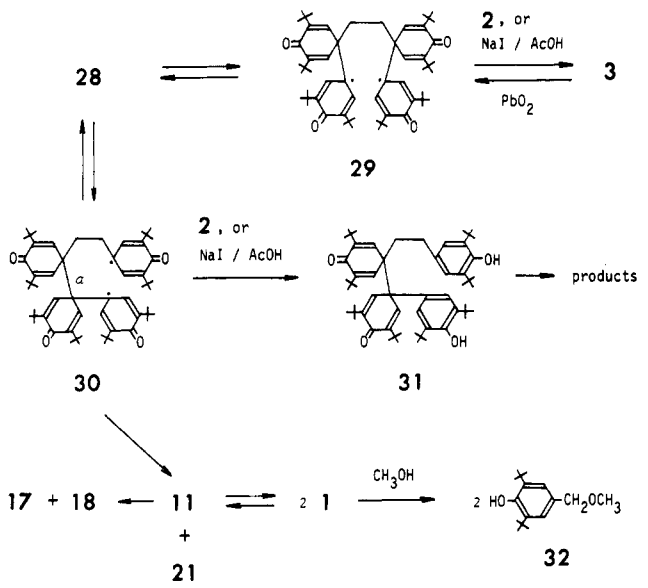
A similar dehydrogenation of **3** with PbO_2 in CH_2Cl_2 gave a product in 83% yield as nearly colorless crystals, mp 100–102 °C dec. The product was unstable in the solid state and in solution and was sensitive to diffused light. Microanalytical data and the IR spectrum (lack of phenolic hydroxyl and presence of dienone bands) were compatible with quarterspiro-dienone structure **28**. Product identi-



28

fication by ^1H NMR spectroscopy was, however, not straightforward. The spectrum ($CDCl_3$) exhibited relatively broad signals at δ 7.26 (s, 2 H), 7.19 (s, 2 H), 6.26 (d, 2 H, J = 3 Hz), 5.97 (d, 2 H, J = 3 Hz), 2.4–2.7 (m, 2 H), and 1.7–2.1 (m, 2 H), as well as relatively narrow singlets at δ 1.34 (36 H), 1.09 (18 H), and 0.91 (18 H). The spectrum is presumed to reflect that conformational flexibility of the cyclohexane ring in **28** is limited due to substitution by the bulky dienone groupings. Protons on the dienone rings and those of tertiary butyl groups are either deshielded (resonating at δ 7.26 and 7.19 and at δ 1.34, respectively) or shielded (resonating at δ 6.26 and 5.97

Scheme III

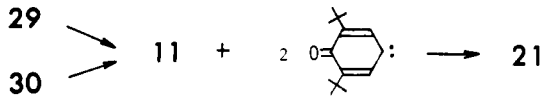


and at δ 1.09 and 0.91, respectively) more than those protons in a number of other 2,6-di-*tert*-butylcyclohexa-2,5-dien-1-ones. These deshieldings and shieldings may be caused by the mutual proximity of the dienone rings, but the detail awaits closer examination. In addition, small signals appeared in the spectrum, due to products of decomposition of **28** in the solution. Crowded molecule **28** is novel in that it holds two kinds of C–C bond (bonds *a* and *b* in the structure) which connects the dienone rings and is likely to be susceptible to homolytic rupture. Compound **28** was allowed to decompose spontaneously in hexane (0.014 M) at 30 °C for 10 h. After evaporation of the reaction mixture, **17**, **18**, and **21** (90%) were principally obtained. They may have been formed by fission of bond *a* in **28**, degradation of the resultant biradical **30** by rupture of the remaining bond *a* to give biradical **11** and **21**, and subsequent disproportionation of the **11** (Scheme III). The decay of **28** in $CDCl_3$ (0.13 M) at 30 °C was also studied by ^1H NMR spectroscopy. The signals due to **28** disappeared from the spectrum in ca. 8 h. Rather unexpectedly, the products were found to consist almost exclusively of quinone methide **1** (1.7 mol/mol **28** employed) and **21** (0.9 mol/mol **28** employed). Signals ascribable to **17** or **18** were hardly detectable. The net process is

$$28 \rightarrow 21 + 21$$

The decay of **28** in MeOH at 30 °C yielded **21** (0.9 mol/mol **28** employed) and benzyl methyl ether **32** (1.6 mol/mol **28** employed) produced by addition of the solvent to **1**. It is therefore suggested that **11** under the conditions dissociated to give **1** rather than disproportionated to give **17** and **18**. In other words, the dimerization of quinone methide **1** is reversible. Compounds **17** and **18** obtained from the disintegration of **28** in hexane, described above, appear to have been produced by the decay of product **1** during the concentration of the mixture after the reaction. Further credence to this reversibility was given by dehydrogenation of **18** with PbO_2 in CH_2Cl_2, which generated **1** as indicated by TLC. Addition of MeOH to the solution containing the **1** provided **32** (1.7 mol/mol **18** employed).

An alternative pathway for the formation of **21** (and **11**) from the decay of **28** involves dimerization of carbene **33** derived from **30** and/or biradical **29**, the product of dissociation of bond *b* in **28**



33

Carbene **33** in the singlet and/or triplet states is a very reactive species and undergoes insertion or addition reaction with benzene, cyclohexane, CCl_4, tetrahydrofuran, or 2-butene.[10] The decay of **28** in hexane or MeOH described above, or that in cyclohexene which afforded **21** in 91% yield, gave no indication of formation of products ascribable to reactions between **33** and the solvents. The results, however, may not mean that fission of bond *b* in **28** to give **29** was not taking place. The decay of **28** in the presence of **2** (5 mol equiv) in hexane at 30 °C gave **3** albeit in low yield (12%). Treatment of **28** with NaI/AcOH also afforded **3** (12%). In these reactions with the reductants, bis-dienone **31** derived from **30** was not obtained, possibly due to its instability under the conditions, although products were not obtained either which could be recognized as those specifically derived from **31**. In summary, **28** in solution dissociates to give both **29** and **30**, and **30** is degraded into **11** and **21** without intermediacy of **33**.

Experimental Section

^1H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ at 60 or 90 MHz and 22.5 MHz, respectively. IR spectra were taken in $CHCl_3$. UV spectra were measured in cyclohexane. Column chromatography was conducted by using Merck SiO_2 60. When products were eluted as a mixture, their contents were estimated by ^1H NMR spectroscopy. TLC was run on SiO_2.

Reaction of Quinone Methide 1 and Phenol 2. To a stirred solution (ca. 6 °C) of benzyl bromide **9**[11] (1.196 g, 4.00 mmol) in pentane (200 mL) was added a solution of Et_3N (404 mg, 4.00 mmol) in pentane (20 mL) over a period of ca. 3 min. After standing for a few minutes, the mixture containing **1** was filtered into a flask containing a solution of **2** (824 mg, 4.00 mmol) in pentane (45 mL) (run 1, Table I) or in a solvent mixture of pentane (40 mL) and Et_3N (5 mL) (run 2, Table I). The mixture was concentrated to a small volume (ca. 20 mL) by evaporation at atmospheric pressure (bath temperature, 45 °C). The concentrate was let stand in a capped bottle at 30 °C for 20 h and evaporated under reduced pressure to give a residual mixture of products.

The reaction in DMSO was conducted in the manner described above except that **1** was generated in benzene and the solution was added to a solution of **2** in DMSO (15 mL) and that the mixture was concentrated to a small volume (ca. 15 mL) under reduced pressure. The reaction mixture was poured into water and extracted with petroleum ether. The extract was washed with water, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to leave a residual mixture of products.

The residue was chromatographed on SiO_2 (60 g) as follows.

In Pentane (run 1, Table I). The column was eluted with petroleum ether. The first fraction gave **2** (192 mg, 23% recovery) as colorless crystals. The second fraction afforded 4,4′-dihydroxybiphenyl **20** (170 mg) as yellow crystals: light yellow crystals from diisopropyl ether, identical with an authentic sample[12] (^1H NMR, IR, and TLC); mp 185–187 °C (lit.[12] mp 185 °C). The third fraction gave a crystalline mixture of **20** (0.31 g, 59% in total) and 1,2-bis(4-hydroxyphenyl)ethane **18** (0.29 g). The fourth fraction provided a crystalline mixture of **18** (0.29 g, 66% in total) and bis(4-hydroxyphenyl)methane **24** (0.11 g, 6%). The mixture was washed with MeOH to isolate **18** (0.21 g): light yellow crystals from diisopropyl ether, identical with an authentic sample[13] (^1H NMR, IR, and TLC); mp 165–168 °C (lit.[13] mp 167–168

(10) (a) Pirkle, W. H.; Koser, G. F. *Tetrahedron Lett.* **1968**, 3959. (b) Huček, A. M.; Barbas, J. T.; Leffler, J. E. *J. Am. Chem. Soc.* **1973**, *95*, 4698.

(11) Cook, C. D.; Nash, N. G.; Flanagan, H. R. *J. Am. Chem. Soc.* **1955**, *77*, 1783.

(12) Kharasch, M. S.; Joshi, B. S. *J. Org. Chem.* **1957**, *22*, 1439.

(13) Omura, K. *J. Org. Chem.* **1984**, *49*, 3046.

°C). The MeOH filtrate was evaporated, and the residue was chromatographed (SiO_2, 70 g). Elution with petroleum ether gave a yellow oil, which was crystallized from hexane to provide **24** (73 mg) as pale yellow crystals, identical with a commercially available sample of **24** (from Tokyo Kasei) (^1H NMR, IR, and TLC); mp 155–156.5 °C (lit.[14] mp 154 °C). Continued elution of the first column with petroleum ether/benzene (10:1) afforded a crystalline mixture containing 4,4′-diphenoquinone **21** (36 mg, 4%). Further elution gave a crystalline mixture, which was washed with MeOH to afford 4,4′-stilbenequinone **17** (35 mg, 4%) as reddish orange crystals, identical with an authentic sample[15] (^1H NMR, IR, and TLC); mp 309–312 °C (lit.[15] mp 310–311 °C).

In Et_3N/Pentane (run 2, Table I). The column was eluted with petroleum ether to give successively **2** (355 mg, 43% recovery), **20** (8 mg, 1%), **18** (0.30 g, 34%), **24** (7 mg, 0.4%), and **21** (26 mg) as single components or as mixtures. Elution with petroleum ether/benzene (10:1) afforded **21** (80 mg, 13% in total): reddish brown crystals from benzene; identical with an authentic sample[13] (^1H NMR, IR, and TLC); mp 246–247 °C (lit.[12] mp 246 °C). Further elution provided 4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-4-[2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethyl]-2,6-di-*tert*-butylcyclohexa-2,5-dien-1-one (**10**) (686 mg, 53%) as a yellow oil, which solidified upon trituration with MeOH. Pale yellow crystals from hexane: mp 164.5–166.5 °C dec; ^{13}C NMR δ 186.92, 152.61, 152.04, 146.25, 145.89, 136.02, 135.96, 132.56, 132.02, 124.62, 123.22, 47.41, 39.32, 34.85, 34.64, 34.31, 30.88, 30.34, 29.63; IR 3615, 1652, 1628 cm^{-1}; UV 274 nm (log ε 3.82), 233 (4.38), 205 (4.88). For the ^1H NMR spectrum (90 MHz), see the text. Anal. Calcd for $C_{44}H_{66}O_3$: C, 82.19; H, 10.35. Found: C, 82.18; H, 10.37. Elution with benzene yielded bis-dienone **3** (152 mg, 9%) as orange crystals: colorless crystals from $CHCl_3$/MeOH, mp 263–265 °C (lit.[2] mp 264–265 °C). The ^1H NMR and IR spectra were compatible with those reported for **3**.[2]

In DMSO. Chromatography conducted in the manner described above for run 2 (Table I) afforded successively **2** (465 mg, 56% recovery), **20** (18 mg, 2%), **18** (0.21 g, 24%), **24** (0.12 g, 7%), **20** (0.10 g, 12%), **10** (0.19 g, 15%), dienone **4** (103 mg, 8%), and **3** (40 mg, 2%).

Reaction of Quinone Methide 1 and Phenol 24. In DMSO. The reaction was conducted and the reaction mixture was worked up in the manner described above for the reaction of **1** and **2** in DMSO, except that **24** (1.696 g, 4.00 mmol) replaced **2**. The crystalline residue was washed with diisoproyl ether to afford **4** (1.200 g) as pale yellow crystals; mp 152–155 °C (lit.[3] mp 152–154 dec). The ^1H NMR and IR spectra were compatible with those reported for **4**.[3] The filtrate was evaporated, and the residue was chromatographed (SiO_2, 25 g). Elution with petroleum ether/benzene (10:1) yielded a crystalline mixture of **18** (0.13 g, 15%) and **24** (0.48 g, 28% recovery). Further elution afforded a crystalline mixture, which was washed with diisopropyl ether to furnish an additional crop of **4** (221 mg, 55% in total).

In Et_3N/Pentane. The reaction was conducted in the manner described above for run 2 (Table I), except that **24** (1.696 g, 4.00 mmol) replaced **2**. Chromatography (SiO_2, 40 g) of the residue gave successively **18** (0.63 g, 72%), **24** (0.91 g, 54% recovery), dienone **25** (0.53 g, 31%), **17** (80 mg, 9%), and **4** (0.27 g, 11%). A petroleum ether fraction provided deep orange crystals (237 mg), which consisted exclusively of **25**: deep yellow crystals from hexane, identical with an authentic sample[14] (^1H NMR, IR, and TLC); mp 159–160 °C (lit.[14] mp 158–159 °C).

Reaction of Quinone Methide 1 and Phenols 2 and 6. The reaction was conducted in the manner described above for runs 1 or 2 (Table I), except that **2** (824 mg, 4.00 mmol) and **6** (880 mg, 4.00 mmol) replaced **2** alone.

In Et_3N/Pentane. Chromatography (SiO_2, 50 g) of the residue gave successively **2** (recovery) and **6** (recovery), **18**, dienone **8** (0.62 g, 37%), **21**, **10**, and **3**. A petroleum ether fraction provided light yellow crystals (322 mg), which consisted exclusively of **8**: colorless crystals from diisopropyl ether, identical with an authentic sample[4] (^1H NMR, IR, and TLC); mp 158–159 °C (lit.[4] mp 157–158 °C).

In Pentane. Chromatography of the residue provided **8** (13 mg, 0.8%). The products obtained from run 1 (Table I) were also obtained by column chromatography.

Dehydrogenation of Biphenols. A mixture of a biphenol and PbO_2 in CH_2Cl_2 was stirred in a screw-capped bottle for 30 min at ice-bath temperature. The reaction mixture was filtered, and the filtrate was evaporated under reduced pressure (bath temperature, <10 °C) to leave a residue.

Biphenol 10. The reaction was conducted with **10** (1.200 g, 1.87 mmol), PbO_2 (3.8 g), and CH_2Cl_2 (20 mL). The oily residue solidified when triturated with MeOH. The solid was washed with hexane to provide terspiro-dienone **27** (762 mg, 64%). Pale yellow crystals from hexane: mp 160–161 °C dec; ^1H NMR (90 MHz) δ 6.57 (s, 4 H), 6.43 (s, 2 H), 2.55 (s, 4 H), 1.18 (s, 36 H), 1.13 (s, 18 H); ^{13}C NMR δ 187.04, 184.86, 148.22, 148.07, 141.33, 138.82, 67.93, 55.70, 36.61, 35.15, 35.12, 34.88, 29.51, 29.30; IR 1654, 1632 cm^{-1}; UV 263 nm (log ε 4.28), 239 (4.25). Anal. Calcd for $C_{44}H_{64}O_3$: C, 82.45; H, 10.07. Found: C, 82.51; H, 10.07.

Biphenol 3. The reaction was conducted with **3** (846 mg, 1.00 mmol), PbO_2 (3.8 g), and CH_2Cl_2 (35 mL). The crystalline residue was washed with cold (ca. 2 °C) hexane to afford quarterspiro-dienone **28** (701 mg, 83%) as pale yellow crystals: mp 100–102 °C dec; IR (KBr disc) 1664, 1631 cm^{-1}. For the ^1H NMR spectrum (90 MHz), see the text. Anal. Calcd for $C_{58}H_{84}O_4$: C, 82.41; H, 10.02. Found: C, 82.46; H, 10.23. Compound **28** turned blue-green when exposed to diffused light.

Biphenol 18. The reaction was conducted with **18** (200 mg, 0.46 mmol), PbO_2 (0.69 g), and CH_2Cl_2 (20 mL). The reaction mixture, which contained **1** as indicated by TLC,[16] was filtered into a flask containing MeOH (100 mL). The mixture was allowed to stand overnight at 30 °C and evaporated under reduced pressure. The residue was chromatographed on SiO_2 plates developed with petroleum ether/benzene (1:1), giving **17** (6 mg, 3%) and methyl ether **32** (189 mg, 83%). Colorless crystals from diisoproyl ether, identical with an authentic sample[13] (^1H NMR, IR, and TLC); mp 98–99 °C (lit.[14] mp 99.5 °C).

Decay of Spirodienones. Spirodienone 27 (Table II). A solution of **27** (320 mg, 0.50 mmol) in a solvent (3.5 mL) containing **2** was kept at 60 °C in a screw-capped bottle. Run 6 was conducted in hexane (3.5 mL) containing Et_3N (120 mg). The reaction mixture was evaporated under reduced pressure, and the residue was chromatographed (SiO_2, 20 g). The reaction mixture in run 6 was filtered to give **3** (157 mg). An additional crop of **3** (29 mg, 44% in total) was recovered from the filtrate by chromatography.

Spirodienone 28. A portion of a solution of **28** (86 mg, 0.10 mmol) and pentachloroethane (PCE) (88 mg) in $CDCl_3$ (0.8 mL) containing TMS was transferred to an NMR tube, and the progress of decay of the **28** was followed by ^1H NMR spectroscopy. As the signals due to **28** diminished, singlets grew which were ascribable to **1** (δ 6.87, 5.70, and 1.27)[4] and **21** (δ 7.64 and 1.35). After ca. 8 h, the signals due to **28** disappeared from the spectrum. The yields of **1** and **21** were estimated to be 1.7 and 0.9 mol/mol **28** employed, by comparing the integrated peak area of a singlet at δ 6.05 due to PCE with those of the singlets at δ 5.70 and 7.64, respectively.

A solution of **28** (60 mg, 0.07 mmol) in hexane (5 mL) was allowed to stand in a screw-capped bottle at 30 °C for 10 h. The reaction mixture, containing no **28** as indicated by TLC, was evaporated. Chromatography (SiO_2, 6 g) of the residue provided **18** (3 mg), **21** (26 mg, 90%), and **17** (7 mg). The same reaction conducted in cyclohexene afforded **21** (26 mg, 90%) as well as small amounts of **17** and **18**.

A solution of **28** (100 mg, 0.12 mmol) in MeOH (50 mL) was kept overnight at 30 °C. The reaction mixture was filtered to give **21** (29 mg). The filtrate was evaporated, and the residue was chromatographed on a SiO_2 plate developed with petroleum ether/benzene (1:1), giving an additional crop of **21** (15 mg, 91% in total) and **32** (47 mg, 79%).

A solution of **28** (100 mg, 0.12 mmol) and **2** (124 mg, 0.60 mmol) in benzene (1 mL) was kept overnight at 30 °C. The reaction mixture was evaporated, and the residue was chromatographed (SiO_2, 9 g), giving **2** recovered (89 mg), **20** (9 mg), **18** (42 mg), **21** (55 mg), and **3** (12 mg, 12%). A mixture of **28** (100 mg, 0.12 mmol) and NaI (1.56 g) in AcOH (30 mL) was stirred overnight at 30 °C. The reaction mixture was poured into water and extracted

(14) Kharasch, M. S.; Joshi, B. S. *J. Org. Chem.* **1957**, *22*, 1435.
(15) Fujisaki, T. *Nippon Kagaku Zasshi* **1956**, *77*, 869.

(16) An authentic sample of **1** generated in situ in hexane by the reaction of **9** with Et_3N showed R_f 0.60 on SiO_2 with petroleum ether/benzene (6:1).

with ether. The extract was washed successively with aqueous $NaHSO_3$ (to remove I_2 liberated) and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue afforded **20** (17 mg), **18** (24 mg), **21** (23 mg), and **3** (12 mg, 12%).

Acknowledgment. The author is grateful to Professor Keizo Naya and Mr. Keiji Hirota (Kwansei Gakuin University) for the measurement of NMR spectra with a JEOL EX-90 spectrometer. He also thanks Mr. Hiroshi Nagao for technical assistance. Valuable comments by the reviewer are gratefully acknowledged.

Registry No. **1**, 2607-52-5; **2**, 128-39-2; **3**, 98543-00-1; **4**, 62078-82-4; **6**, 128-37-0; **8**, 14387-13-4; **9**, 2091-51-2; **10**, 137649-09-3; **17**, 809-73-4; **18**, 1516-94-5; **20**, 128-38-1; **21**, 2455-14-3; **24**, 118-82-1; **25**, 4359-97-1; **27**, 137649-10-6; **28**, 137668-00-9.

Highly Selective Monoacylation of Symmetric Diols Catalyzed by Metal Sulfates Supported on Silica Gel

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Several 1,*n*-diols, ranging from 1,2-ethanediol to 1,16-hexadecanediol, were monoacylated with high selectivity by reaction with esters in the presence of metal sulfates or hydrogen sulfates, like $Ce(SO_4)_2$ and $NaHSO_4$, supported on silica gel. Symmetrical secondary diols were also selectively monoformylated, by reaction with ethyl formate. This method of selective esterification is simple and practical. The yield of monoester depends upon both the composition and the volume of the solvent (an ester/alkane mixture). Unsupported $NaHSO_4$ also catalyzed monoacylation, but the selectivity was less than in monoacylations catalyzed by the supported reagent. The selectivity can be explained by the following reasons: (1) monoacylated products are formed selectively because the diol, but not the monoester, is preferentially adsorbed on the surface of the catalysts, where esterification then occurs, and (2) thin diol layers are formed on the surface of the catalysts due to limited solubility of the diols in the solvent.

Introduction

It is important for organic chemists to develop methods that permit the selective protection or functionalization of multiple identical functional groups that exist in similar chemical environments. In some cases the monoprotection of 1,*n*-diols can be achieved by careful control of the reaction conditions;[1] by continuous extraction;[2] by the use of alumina,[3] phase-transfer catalysts,[4] or insoluble polymer supports;[5] or via the formation of cyclic compounds.[6] The use of supported reagents often has advantages over that of their homogeneous counterparts.[7] During a study of the dehydration of alcohols catalyzed by metal sulfates and hydrogen sulfates supported on silica gel,[8] we found that the alcohols were acylated, via transesterification, when esters were used as solvents[9,10] and that 1,*n*-diols were monoacylated.[11] Here we describe the selective monoacylation in more detail.

$$HO(CH_2)_pOH + R^1CO_2R^2 \xrightarrow{M_m(SO_4)_n\text{-}SiO_2} R^1CO_2(CH_2)_pOH + [R^1CO_2(CH_2)_pOCOR^1] \quad (1)$$

Results and Discussion

Selective Monoacylation of Symmetric Diols. The monoacylations were performed by heating together a diol (1 mmol), $M_m(SO_4)_n$–SiO_2 catalyst (3 mmol metal sulfate/g SiO_2), and an ester/hexane (or octane) mixture. The reactions were monitored by TLC and GLC. Table I shows that all of the 1,*n*-diols that were examined, ranging from 1,2-ethanediol to 1,16-hexadecanediol, gave the corresponding monoesters in acceptable yields.[12] Lowering the reaction temperature or reducing the amount of catalyst led to an increase in selectivity, although longer reaction times were necessary. Symmetrical secondary diols were also monoformylated, with moderate selectivity, by reaction with ethyl formate.[13]

Rationalization of the Selectivity. Figure 1 shows the yields of the products as a function of time for the acylation of 1,4-butanediol by methyl isobutyrate. The

(1) (a) Wilkinson, S. G. In *Comprehensive Organic Chemistry*; Stoddart, J. F., Ed.; Pergamon Press: New York, 1979; Vol. 1, p 681. (b) Furhop, J.; Penzlin, G. *Organic Synthesis*; Verlag Chemie: Weinheim, 1983; p 143.
(2) Babler, J. H.; Coghlan, M. J. *Tetrahedron Lett.* **1979**, *22*, 1971.
(3) (a) Ogawa, H.; Chihara, T.; Taya, K. *J. Am. Chem. Soc.* **1985**, *107*, 1365. (b) Ogawa, H.; Ichimura, Y.; Cihara, T.; Teratani, S.; Taya, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2481. (c) Ogawa, H.; Chihara, T.; Teratani, S.; Taya, K. *J. Chem. Soc., Chem. Commun.* **1986**, 1337.
(4) Zerda, J. D. L.; Barak, G.; Sasson, Y. *Tetrahedron.* **1989**, *29*, 1533.
(5) Leznoff, C. C. *Acc. Chem. Res.* **1978**, *11*, 327.
(6) (a) Takasu, M.; Naruse, Y.; Yamamoto, H. *Tetrahedron Lett.* **1988**, *29*, 1947. (b) Takano, S.; Akiyama, M.; Sato, S.; Ogasawara, K. *Chem. Lett.* **1983**, 1593.
(7) *Preparative Chemistry Using Supported Reagents*; Laszlo, P., Ed.; Academic Press: San Diego, 1987.
(8) Nishiguchi, T.; Kamio, C. *J. Chem. Soc., Perkin Trans. 1* **1989**, 707.
(9) Nishiguchi, T.; Taya, H. *J. Chem. Soc., Perkin Trans. 1* **1990**, 172.
(10) For examples of transesterifications catalyzed by alumina and references to transesterification catalyzed by acids and bases, see: (a) Posner, G. H.; Okada, S. S.; Babiak, K. A.; Miura, K.; Rose, K. *Synthesis* **1981**, 789. (b) Posner, G. H.; Okada, M. *Tetrahedron Lett.* **1981**, *22*, 5003.
(11) Nishiguchi, T.; Taya, H. *J. Am. Chem. Soc.* **1989**, *111*, 9102.
(12) Changing the identity of the catalyst did not significantly affect the selectivity of the reaction as long as the catalytic activity of the salt was high. In the $Fe_2(SO_4)_3$-catalyzed acylation of 1,4-butanediol, changing the solid support from silica gel to neutral alumina, Celite-535, or powdered 3A molecular sieves led both to a decrease in activity of the catalyst and a decrease in selectivity.
(13) No products other than esters were formed during the reaction of secondary diols in ethyl formate/hexane and of primary diols in any solvent. However, substantial quantities of olefins were produced, along with the expected esters, during reaction of secondary diols in EtOAc/hexane.

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