Table III. Preparation of (*E*)-*N*-(4-aryl-3-butenyl)phthalimides, 8-12

product	Ar	method[a]	mp, °C	*Z*:*E*[b]
8	Ph	A	146.5-147.5	
9	*p*-ClPh	B	130.5-132	11:89
10	*p*-MeOPh	B	136.5-138	30:70
11	*p*-MePh	B	123.5-124	4:96
12	*m*-NO$_2$Ph	C	138-140	15:85

[a] Method A: via the cinnamaldehyde.[24] Method B: via iodine-catalyzed isomerization in pentane. Method C: via iodine-catalyzed isomerization in benzene. [b] Isomer ratio in equilibrated product (by gas chromatography), before purification by recrystallization (for methods B and C).

Other Wittig Reactions. The results of the other Wittig reactions of 7 (X = H) or 7 (X = OMe) with benzaldehyde and with substituted benzaldehydes are presented in Table II.

Calculation of Absolute Yields of Alkenes from GC Peak Areas. In order to convert peak areas to absolute yields, it was necessary to prepare pure cis and trans isomers of each product, so that solutions of standard concentration could be analyzed. In all instances, pure cis isomer was prepared by recrystallizing a portion of the reaction product from ethanol (until only one peak appeared in a gas chromatogram). Pure *E* isomer was produced by two methods: (a) through reaction of an appropriate *trans*-4-aryl-3-butenylamine hydrochloride with phthalic anhydride[24] or (b) iodine-catalyzed isomerization of the cis isomer to the more thermodynamically stable trans form.

Isomerization of the *cis*-*N*-(4-aryl-3-butenyl)phthalimides to the trans isomers proved to be the most convenient means whereby the latter compounds could be obtained. Thus, it was found that, for **9**–**11**, irradiation (with a 200-W visible lamp) of a pentane solution of the cis isomer, in the presence of a catalytic amount of iodine, afforded an equilibrium mixture of cis and trans product, in which the trans isomer was the principal component. Recrystallization of the solid product from ethanol then afforded pure trans product (recrystallization was continued until the sample displayed only one peak by gas chromatography). Compound **12** was only sparingly soluble in pentane; therefore, the isomerization of this compound was accomplished in benzene. The results are shown in Table III.

With pure samples of the cis and trans isomer of each product available, gas chromatographic standards were accurately prepared so that peak areas could be interpreted as absolute yields. The relative response ratio was calculated from a minimum of six data points by linear regression line analysis (each correlation coefficient having a value of $r = 1.00$). The isomer distribution data presented in Tables I and II have been corrected in this manner.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research.

Registry No. 7 (X = H), 7743-29-5; 7 (X = OMe), 84812-12-4; (*E*)-8, 74592-04-4; (*Z*)-8, 74591-93-8; (*E*)-**9**, 74592-05-5; (*Z*)-**9**, 74591-94-9; (*E*)-**10**, 84812-13-5; (*Z*)-**10**, 74591-96-1; (*E*)-**11**, 84812-14-6; (*Z*)-**11**, 74591-95-0; (*E*)-**12**, 84812-15-7; (*Z*)-**12**, 74591-98-3; PhCHO, 100-52-7; *p*-ClC$_6$H$_4$CHO, 104-88-1; *p*-MeOC$_6$H$_4$CHO, 123-11-5; *p*-MeC$_6$H$_4$CHO, 104-87-0; *m*-NO$_2$C$_6$H$_4$CHO, 99-61-6; *N*-(3-bromopropyl)phthalimide, 5460-29-7; (2,6-dimethoxyphenyl)diphenylphosphine, 66417-43-4.

Reduction of Unsymmetrical Benzils Using Sodium Dithionite

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Contrary to a previous report, reduction of unsymmetrical benzils by sodium dithionite (sodium hydrosulfite) in general yields a mixture of isomeric benzoins. Whereas the reduction of aldehydes and ketones by dithionite apparently takes place by a nucleophilic addition mechanism, the reduction of benzils proceeds by an electron-transfer mechanism. The inital product of the reduction is the (*Z*)-α,α′-stilbenediol which is produced stereospecifically. The ultimate benzoin products, then, result from the two different modes of ketolization of the stilbenediol intermediate.

Sodium dithionite (sodium hydrosulfite) has long been recognized as a powerful reducing agent for a variety of functional groups.[1] Synthetic and mechanistic studies of the reduction of simple carbonyl compounds by this reagent have been a much more recent development and have received considerable attention in the past few years.[2]

In contrast to the reduction of aldehydes and ketones, reduction of benzil to benzoin with sodium dithionite has been known for some time.[3] Extension of the reaction to unsymmetrical benzils (**1**) was reported by van Es and Backeberg[4] to proceed with quantitative and exclusive reduction at the most electron-deficient carbonyl group. Thus, only benzoin **2** was obtained when X was electron withdrawing and only benzoin **3** when X was electron releasing (eq 1).

Table I. Benzoin Product Yields from Dithionite Reduction of Unsymmetrically Substituted Benzils

		% yield	
benzil	X	2	3
1a	Cl	60	40
1b	CH$_3$	40	60
1c	OCH$_3$	37	63
1d	OH	27	73

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(1) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; p 1081.

(2) (a) deVries, J. G.; van Bergen, T. J.; Kellogg, R. M. *Synthesis* **1977**, 46. (b) Minato, H; Fujie, S.; Okuma, K.; Kobayaski, M. *Chemistry Lett.* **1977**, 1091. (c) Camps, F.; Coll, J.; Riba, M. *J. Chem. Soc., Chem. Commun.* **1979**, 1080. (d) de Vries, J. G.; Kellogg, R. M. *J. Org. Chem.* **1980**, *45*, 1426. (e) Krapcho, A. P.; Seidman, D. A. *Tetrahedron Lett.* **1981**, *22*, 179. (f) Chung, S.-K. *J. Org. Chem.* **1981**, *46*, 5457.

(3) Grandmougin, E. *J. Prakt. Chem.* **1907**, *76*, 124.

(4) van Es, T.; Backeberg, O. G. *J. Chem. Soc.* **1963**, 1371.

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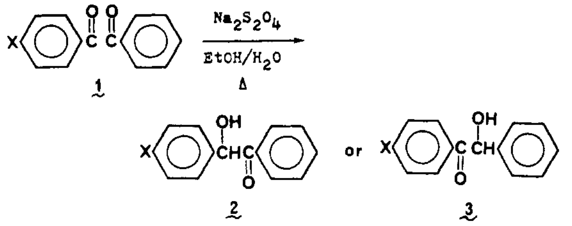


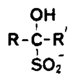
(1)

The need for a sample of 4-chlorobenzoin[5] (**2a**) in connection with another study prompted us to apply dithionite reduction to 4-chlorobenzil (**1a**). To our surprise and in complete contrast to the literature,[4] analysis of the reaction mixture revealed that both isomers **2a** and **3a** were formed in 60% and 40% yields, respectively.

This result prompted us to examine the reductions of other unsymmetrical benzils with sodium dithionite, and the results of our study are given in Table I. In all cases, essentially a quantitative conversion to benzoin products was obtained. Percent yields of the benzoin isomers were determined by NMR analysis of the crude product mixtures, with 4- and 4′-isomers being identified by comparison with NMR spectra of authentic samples.

It is apparent from the data that only *predominant* reduction occurs at the most electron-deficient carbonyl since very substantial quantities, i.e., 27–40%, of the other isomer were produced.

The mechanism of dithionite reductions of aldehydes and ketones is not without controversy, although recent evidence favors nucleophilic addition of either dithionite itself[2d] or a sulfur dioxide dianion or its equivalent,[2f] leading to an α-hydroxy sulfinate (**4**) which ultimately eliminates sulfur dioxide and is protonated to produce the alcohol. The possibility also exists for the reaction to proceed by electron transfer from sulfur dioxide radical anions (**5**) generated thermally[2e,6] (eq 2).



$\mathrm{R{-}\overset{OH}{\underset{SO_2^-}{C}}{-}R'}$

4

$$S_2O_4^{=} \xrightarrow{\Delta} 2\ SO_2^{\dot{-}} \qquad (2)$$

5

In the hope of gaining some mechanistic insight into the reduction of benzils, we have examined some of the more salient features of the reaction.

First of all, the thermodynamically less stable isomer 4-methylbenzoin (**2b**) was recovered unchanged when treated under the reaction conditions, thus eliminating equilibration as a factor in determining product ratios.

Second, the question of stoichiometry was considered. Previous reports[3,4,7] of the reduction of benzils with dithionite have utilized a substantial excess of the reagent. Determination of the overall stoichiometry was hampered by the well-known ability of dithionite to react with oxygen[8] and by utilization of a commercial reagent of unknown assay. Therefore, the reaction of 1 molar equiv of sodium dithionite[9] (88% assay[10]) with 1 molar equiv of benzil was conducted under nitrogen. Since nearly an equivalent amount, i.e., 83% yield, of benzoin was produced, the dithionite to benzil stoichiometry appears to be 1:1.

The effect of pH on the reaction was a third consideration. The reduction of aldehydes and ketones by dithionite is reported to proceed only in the presence of sufficient sodium bicarbonate to maintain a high pH.[2a] By contrast, the reduction of benzils proceeds rapidly in unbuffered media,[4] the final pH of the reaction medium being about pH 5. Reduction of 4-methylbenzil (**1b**) in the presence of a 6 molar excess of sodium bicarbonate afforded a benzoin product mixture of 63% of the 4′-isomer (**3b**) and 37% of the 4-isomer (**2b**). Since a 60:40 ratio (Table I) was obtained in the absence of the base, it appears that pH has substantially no effect on the reduction of benzils and the ratio of benzoin products formed.

Finally, the question of whether the reduction of benzils proceeds by nucleophilic attack or by an electron-transfer mechanism was addressed.

When the reduction of benzil was conducted in the NMR probe at 80 °C, a rapid transformation to benzoin ensued, and CIDNP effects were observed. That is, both emission and enhanced absorption resonances associated with the benzoin product were produced, although reproducibility with the heterogeneous reaction was poor at best. This result indicated that radical intermediates were involved. Whether these intermediates provided the major, as opposed to a minor, pathway to product in the reaction could not be ascertained at this point.

Examination of the reaction by ESR resulted in ready detection of the sulfur dioxide radical anion (**5**) at room temperature, but no benzil-derived radicals could be detected. One problem is that while the benzil radical anion is quite stable in solvents like DMF[11] it will, in all likelihood, be quickly protonated and further reduced in the dithionite–ethanol–water medium. What was surprising about the ESR experiment, as evidenced by TLC, was that the reduction did take place and proceed to completion at room temperature. This is in sharp contrast to temperatures in excess of 85 °C that are required for reduction of aldehydes and ketones.[2d]

This result prompted us to reexamine the reaction in the NMR probe at room temperature to determine whether any intermediates might be detectable at this lower temperature. Within the first 5–8 min of the reaction, the benzil resonances totally disappeared concomitant with the appearance of a single, relatively sharp, intense resonance at δ 7.18, suggesting a fairly symmetrical intermediate. This species was then rather slowly, i.e., 91% conversion in 150 min, transformed into benzoin. It was also possible to obtain a ^{13}C NMR spectrum of the intermediate. Recording the FT spectrum at 15-min intervals revealed that, in addition to a multiplet of aromatic carbon resonances, two new quaternary carbon resonances appeared at 135.1 and 135.9 ppm which also disappeared with time.

The electrochemical reduction of benzil in ethanol–water media has been studied by several workers.[12-14] They have shown rather convincingly that the intermediate products of the reduction are the (*E*)- and (*Z*)-α,α'-stilbenediols (**6** and **7**, eq 3).

Intermediacy of **7**, in particular, seems reasonable from the spectral data described above for the intermediate in the dithionite reduction. In addition, both the ^1H and ^{13}C

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[5] The nomenclature for substituted benzoins is somewhat in disarray in the literature. We have adopted the nomenclature system depicted under "Benzoin" in: "CRC Handbook of Chemistry and Physics: College Edition"; CRC Press: Cleveland, OH, 1980. Here the primed number substituents are located on the benzoyl ring.

[6] Burlamacchi, L.; Guarini, G.; Tiezzi, E. *Trans. Faraday Soc.* **1969**, *65*, 496.

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[8] Creutz, C.; Sutin, N. *Inorg. Chem* **1974**, *13*, 2041.

[9] We express our appreciation to the Fisher Scientific Co. for a gift of sodium hydrosulfite that was prepared in June 1982.

[10] Danehy, J. P.; Zubritsky, C. W.; III. *Anal. Chem.* **1974**, *46*, 391.

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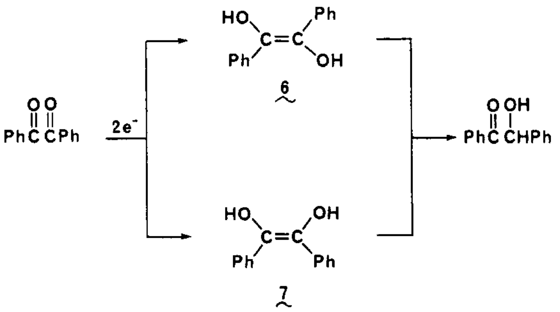
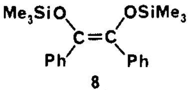


(3)

NMR spectra compare very favorably with those of the bis(trimethylsilyl) derivative[15] 8. The ^1H spectrum for



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8 shows a rather sharp resonance for the aromatic protons centered at δ 7.11 (compared to δ 7.18 for the dithionite intermediate), and the ^{13}C spectrum for 8 has quaternary carbon resonances at 136.9 and 138.3 ppm (compared to 135.1 and 135.9 ppm). Furthermore, the lifetime of the intermediate compares favorably with the reported rates of ketolization for 7 of 2.4×10^{-3} s^{-1} at pH 7.5[14] and 4.5×10^{-5} s^{-1} for 6 at pH 3.6.[12] From the NMR experiment we can estimate $k \approx 3 \times 10^{-4}$ s^{-1} at pH 5 for the dithionite intermediate which interpolates quite well.

The UV spectra of compounds 6 and 7 have been reported by two groups.[13,16] Identification of the *E* isomer 6 is particularly easy due to a rather intense (ϵ 16000) absorption band at 310–318 nm; the UV spectrum of the *Z* isomer 7 is less distinguishable because of interferring absorptions by both benzil and benzoin at 265 nm. Examination of the UV spectrum for the dithionite intermediate showed no absorption band at 310–318 nm for the *E* isomer 6 but a spectrum which was not inconsistent with that reported for the *Z* isomer 7.

The electrochemical oxidation of compounds 6 and 7 has been studied at acidic pH in ethanol–water solution by using a hanging mercury drop electrode.[12] Production of both 6 and 7 from the electrochemical reduction of benzil was found to depend on many factors. When both isomers were produced, however, the oxidation waves were clearly resolved, with the *Z* isomer 7 oxidizing 90 mV more positive than the *E* isomer 6. In Figure 1a is shown the oxidation of the stilbenediols produced by electrolyzing benzil at −1.0 V (Ag–AgCl) at pH 5. Figure 1b shows a similar oxidation after some of the dithionite reduction intermediate has been added. Note that the second peak (the oxidation wave of the *Z* isomer 7) is increased relative to the unspiked system.

With the identification of the stilbenediol as the actual intermediate in the dithionite reduction of benzils to benzoins, some question still remained as to what was the actual reductant in the system. Rinker has shown[17] that acidification of aqueous solutions of sodium formaldehydesulfoxylate (9) results in the formation of the sulfur dioxide radical anion (5, eq 4). Consequently, we

$$\underset{9}{HOCH_2SO_2^-\ Na^+} \xrightarrow{H^+} \underset{5}{SO_2^{\cdot -}} \qquad (4)$$

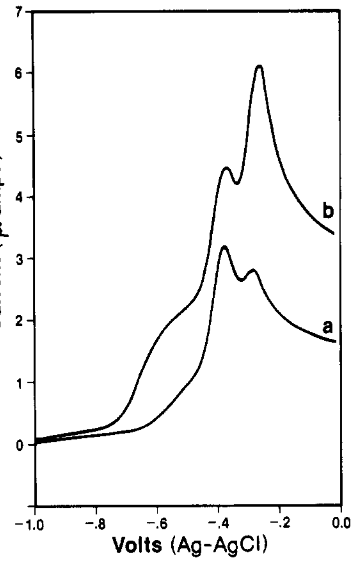


Figure 1. Voltammetry of α,α'-stilbenediols: (a) oxidation of (*E*)- and (*Z*)-α,α'-stilbenediols produced by electrolysis of benzil at −1.0 volt; (b) previous system spiked with dithionite–benzil reduction intermediate.

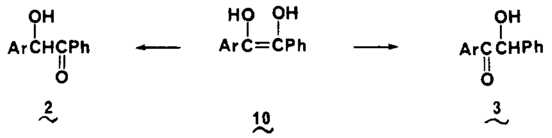
Table II. Substituent Effects on Ketolization of Stilbenediols (10) and on Enolization of *p*-Substituted Deoxybenzoins

X	rel rate 3/2	rel rate enolization[a]
Cl	0.67	0.48
H	1.0	1.00
CH_3	1.5	1.21
OCH_3	1.7	1.65[b]
OH	2.7	
ρ	−1.02	−1.0

[a] Reference 19, substituent on benzoyl group. [b] Value for X = OCH_2CH_3.[19]

attempted to reduce benzil with 9 as the reducing agent and found that the reduction occurred only in the presence of acid. Furthermore, reduction of 4-chlorobenzil (**1a**) with excess 9 in ethanol/1.5 N HCl resulted in a 64:36 molar yield of benzoins **2a** and **3a**, in essentially the same product ratio as that obtained by using dithionite. These results implicate radical anion 5 as the actual reductant in the reaction.

The intermediacy of stilbenediols in the dithionite reduction of benzils now provides a rationale for the production of isomeric product mixtures from unsymmetrical benzils. The relative amounts of benzoins 2 and 3 are simply a reflection of the relative rates of ketolization of intermediate diol 10. Taking the relative rate for the



unsubstituted phenyl group to be equal to 1.0, the relative rates for the various substituents are simply the ratios of the products, 3/2 (Table II). A plot of the σ values[18] for the substituents vs. the logarithm of the relative rates exhibits reasonable linearity (R = 0.984) and yields a reaction constant ρ = −1.02. These results are strikingly

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[15] Unpublished results; an improved synthesis for several bis(trimethylsilyl)enediols is in the process of being submitted for publication.

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Table III

	chemical shift, δ, for carbon							
	1	2,6	3,5	4	1′	2′,6′	3′,5′	4′
calcd	131.3	128.3	115.3	157.4	136.4	128.7	128.4	132.9
obsd	131.53	129.3	116.38	158.13	135.36	129.86	129.70	134.06

similar (Table II) to those obtained by Wiberg[19] for the rates of enolization of substituted deoxybenzoins as determined by acid-catalyzed bromination in 91% acetic acid media.

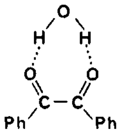
In conclusion, the dithionite reduction of benzils appears to proceed by an electron-transfer mechanism[20] in contrast to the currently accepted nucleophilic addition mechanism[2d,f] with simple aldehydes and ketones. This conclusion is supported by several experimental observations:

(1) Bisulfite is totally unreactive with benzil at room temperature in ethanol–water solution as evidenced by ^{1}H NMR. Since bisulfite would be expected to be of comparable nucleophilicity with dithionite, nucleophilic addition of dithionite to the benzil system is not supported.

(2) The complete absence of rearrangement or cleavage products, commonly found in the reaction of benzils with nucleophilic agents,[21] is also consistent with a nonnucleophilic mechanism.

(3) Sulfur dioxide radical anion (**5**), when generated from a source other than dithionite, is clearly capable of carrying out the reaction as shown by the sodium formaldehydesulfoxylate (**9**)–hydrochloric acid experiment. The lack of reaction in nonacidic media, when **5** is not produced, is also quite discerning.

(4) The initial product of the reaction is the stilbenediol **7**, which along with its isomer **6** is also a product of the electrochemical reduction of benzil. Just why the dithionite reduction occurs stereospecifically to form **7** is not presently known. It may be that the ethanol–water medium encourages a cisoid benzil conformation because the highly polar solvent would favor dipole formation that would be present only in the cisoid arrangement. Also, structures such as **11**, which have been proposed to be important in photochemical transformations of benzil,[16] may also be important in determining the ultimate stereochemistry.



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(5) CIDNP effects were obtained when the concentration of the radical intermediates leading to **7** and benzoin was sufficiently high, i.e., when the reaction was conducted at 80 °C.

Experimental Section

Melting points were taken by using a Thomas-Hoover capillary melting point apparatus and were not corrected. NMR spectra were obtained unless otherwise stated by using a Varian XL-200 spectrometer operating at 200.056 (^{1}H) or 50.32 MHz (^{13}C). The acquisition parameters for ^{1}H and ^{13}C, respectively, were as follows: spectral width = 3000 and 10 000 Hz; pulse width = 3 and 6 μs; acquisition time = 2.6 and 0.6 s. ESR spectra were obtained by using a Varian Model D4502 EPR spectrometer and a flat-cell arrangement (also available from Varian) for solvents exhibiting high microwave loss. UV spectra were recorded by using a Hitachi-Coleman Model EPS-3T recording spectrophotometer. The electrochemical studies were performed by using a Princeton Applied Research (PAR) Model 174 pulse polargraph, a PAR Model 315A controller, and a PAR Model 303 mercury drop electrode.

Materials. Sodium hydrosulfite (sodium dithionite) and sodium bisulfite were obtained from the Fisher Scientific Co. and were used without further purification. Sodium formaldehydesulfoxylate was used as received from Eastman Organic Chemicals.

4-Chlorobenzil [mp 72–73.5 °C (lit.[22] mp 73 °C)], 4-methylbenzil [mp 29.5–30 °C (lit.[22] mp 31 °C)], and 4-methoxybenzil [mp 58–58.5 °C (lit.[23] mp 62–63 °C)] were prepared by oxidation of benzoin precursors according to the method of Weiss and Appel.[24] 4-Hydroxybenzil [mp 129–130 °C (lit.[25] mp 127–129 °C)] was prepared by hydrobromic acid induced cleavage of 4-methoxybenzil according to a literature method.[25]

Potential benzoin products of the reduction reaction were independently synthesized according to literature methods. The compounds prepared and their physical and NMR spectral data were as follows. **4-Chlorobenzoin**: mp 110–113 °C (lit.[26] mp 116 °C); ^{1}H NMR (CDCl$_3$) δ 4.58 (d, J = 6 Hz, 1 H), 5.95 (d, J = 6 Hz, 1 H), 7.4 (m, 7 H), and 7.9 (m, 2 H). **4′-Chlorobenzoin**: mp 87–88 °C (lit.[26] mp 90–91 °C); ^{1}H NMR (CDCl$_3$) δ 4.44 (d, J = 6 Hz, 1 H), 5.87 (d, J = 6 Hz, 1 H), 7.34 (m, 7 H), 7.86 (d, J = 8 Hz, 2 H). **4-Methylbenzoin**: mp 113–116 °C (lit.[26] mp 116 °C); ^{1}H NMR (CDCl$_3$) δ 2.28 (s, 3 H), 4.5 (d, J = 6.5 Hz, 1 H), 5.96 (d, J = 6.5 Hz, 1 H), 7.4 (m, 7 H), 8.02 (m, 2 H). **4′-Methylbenzoin**: mp 108.5–109 °C (lit.[26] mp 109–110 °C); ^{1}H NMR (CDCl$_3$) δ 2.37 (s, 3 H), 4.5 (br s, 1 H), 5.95 (s, 1 H), 7.3 (m, 7 H), 7.92 (d, J = 8 Hz, 2 H). **4-Methoxybenzoin**: mp 88–89 °C (lit.[27] mp 89 °C); ^{1}H NMR (CDCl$_3$) δ 3.76 (s, 3 H), 4.5 (br s, 1 H), 5.91 (s, 1 H), 6.83 (d, J = 8 Hz, 2 H), 7.5 (m, 5 H), 7.9 (m, 2 H). **4′-Methoxybenzoin**: mp 104.5–105.5 °C (lit.[28] mp 105.5–106.5 °C); ^{1}H NMR (CDCl$_3$) δ 3.82 (s, 3 H), 4.6 (d, J = 6 Hz, 1 H), 5.89 (d, J = 6 Hz, 1 H), 6.86 (d, J = 8 Hz, 2 H), 7.3 (m, 5 H), 7.90 (d, J = 8 Hz, 2 H). **4′-Hydroxybenzoin**: mp 173–174.5 °C (gas evolution) (lit.[29] mp 187–189 °C); ^{1}H NMR ((CD$_3$)$_2$C=O) δ 4.7 (br s, 1 H), 6.09 (s, 1 H), 6.82 (d, J = 8 Hz, 2 H), 7.2 (m, 5 H), 8.06 (m, 2 H), 8.45 (br s, 1 H). Because the melting point was quite low compared with the reported value the ^{13}C NMR spectrum was also obtained in order to corroborate the structure of the compound, and it was found to compare favorably with the calculated spectrum[30] (Table III).

General Procedure for the Dithionite Reductions. The following procedure is essentially that of van Es and Backeberg.[4] The benzil (0.500 g) and absolute ethanol (15 mL) were stirred and heated to reflux. A solution of sodium dithionite (1.5 g) in water (5 mL) was added in one portion, causing precipitation to occur of typically a yellowish solid. The mixture was refluxed briskly for 30 min and allowed to cool, and the now colorless reaction mixture was evaporated to dryness on a rotary evaporator. The benzoin products were extracted into ethyl acetate (50 mL)

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[19] Wiberg, K. B.; Anilin, O.; Gotzke, A. *J. Org. Chem.* **1972**, *37*, 3229.

[20] A referee has pointed out quite rightly that the available experimental evidence does not rigorously exclude a nucleophilic addition mechanism. The reason that an α-hydroxy sulfinate addition product may not have been observed with benzils as opposed to aldehydes and ketones[2d] is because elimination of SO$_2$ would be expected to be very fast because of the "electron sink" of the adjacent carbonyl group.

[21] (a) Benzilic acid and related rearrangements catalyzed by hydroxide and alkoxides: Selman, S.; Easthan, J. F. *Q. Rev., Chem. Soc.* **1960**, *14*, 221. (b) Cyanide-catalyzed rearrangements: Kuebrich, J. P.; Schowen, R. L. *J. Am. Chem. Soc.* **1971**, *93*, 1220.

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Table IV

	chemical shift, δ, for carbon							
	1	2,6	3,5	4	1′	2′,6′	3′,5′	4′
calcd	140.1	127.2	128.3	128.1	127.6	129.8	115.4	162.2
obsd	141.31	128.31	129.4	128.65	126.88	132.50	116.14	163.19

and were dried over anhydrous magnesium sulfate. TLC analysis indicated that conversion to benzoin products was quantitative in all cases. An aliquot (2 mL) was withdrawn, the solvent evaporated, and the residue dissolved in the appropriate solvent for NMR analysis. The ratios of the benzoin products were determined from the integrated areas of certain resolvable resonances in the ^{1}H NMR spectra, with isomer identities being determined by comparison with NMR spectra of authentic samples. These resolvable resonances were the benzylic methine singlets for the chlorobenzoins, the methyl singlets for the methylbenzoins, the methoxy singlets for the methoxybenzoins, and the ortho (to the ring OH) proton doublets for the hydroxybenzoins.

Identification of 4′-Hydroxybenzoin. The reduction of 4-hydroxybenzil was performed on a 5-g scale. A benzoin product mixture weighing 4.69 g (93% yield) was obtained.

This mixture (0.0206 mol) was suspended in water (15 mL), and a standard sodium hydroxide solution (0.986 N, 20.39 mL, 0.0206 mol) was added, causing a slightly yellow solution to be formed. Next, a solution of methanesulfonyl chloride (2.40 g, 0.021 mol) in methylene chloride (25 mL) and tetrabutylammonium bisulfate (0.1 g) were added and shaken; almost immediately the color was removed from the aqueous layer. The mixture was shaken mechanically for 15 min. The organic layer was separated and dried ($MgSO_4$). Removal of the solvent left 6.23 g (99% yield) of the mesyloxy-substituted benzoins as a light brown oil.

A portion of the oil (3.0 g, 0.0098 mol) was dissolved in acetone (25 mL), and a standard sodium hydroxide solution (0.986 *N*, 20.2 mL, 0.0196 mol) was added. The mixture was stirred at room temperature overnight, and the acetone was removed at reduced pressure. A crude separation of the 4-mesyloxy isomer, which was stable to the caustic at room temperature, was effected at this point by extraction with methylene chloride (25 mL). The aqueous layer was acidified with concentrated hydrochloric acid, and the turbid suspension that resulted was extracted with ethyl acetate (50 mL). Washing with aqueous 10% sodium bicarbonate (3 × 25 mL), followed by drying ($MgSO_4$) and removal of the solvent, produced a light brown semisolid weighing 1.35 g. The solid was recrystallized from ethyl acetate/methylene chloride, yielding a white powder weighing 0.7 g (31% yield) and melting at 175–178 °C. The sample was further recrystallized from ethanol/water, yielding colorless needles: mp 180.5–181 °C; IR (Nujol) 3.1, 6.05, 6.25, 7.80, 8.02, 8.31, 8.65, 9.35, 10.25, 11.60, 13.15, 14.45 μm; ^{1}H NMR ($(CD_3)_2C{=}O$) δ 4.88 (br s, 1 H), 6.03 (s, 1 H), 7.87 (d, *J* = 8 Hz, 2 H), 7.35 (m, 5 H), 7.98 (d, *J* = 8 Hz, 2 H); mass spectrum, calcd *m/e* 228.078, obsd 228.076; ^{13}C NMR ($(CD_3)_2C{=}O$) data are given in Table IV.

Reaction Parameter. The reaction parameters of thermodynamic control, reaction stoichiometry, and pH of the reaction were examined.

Thermodynamic Control. 4-Methylbenzoin (**2b**) was subjected to reaction with sodium dithionite under the conditions of the general procedure above and was recovered unchanged.

Reaction Stoichiometry. The reduction of benzil was conducted as described in the general procedure except that 1 equiv (0.414 g, 0.002 38 mol) of sodium dithionite (88% assay[10]) was utilized. Also, the reduction was performed in an atmosphere of nitrogen and with nitrogen-sparged solvents. After the 30-min reflux period, the solvent was removed from an aliquot of the reaction mixture. ^{1}H NMR indicated a molar ratio of benzoin to benzil of 83:17 based on the integration for the methine resonance at δ 5.98 ($CDCl_3$) compared to the total integration for the aromatic protons ortho to the carbonyl group at δ 7.82–8.10.

pH of Reaction. The reduction of 4-methylbenzil (**1b**) was conducted as in the general procedure except that 6 equiv (1.12 g, 0.013 mol) of sodium bicarbonate was also added. NMR analysis of the reaction products indicated a ratio of **3b** to **2b** of 63:37.

Reaction Mechanism. Several studies were directed toward elucidation of the reaction mechanism.

Examination of the Dithionite Reduction of Benzil in the NMR Probe. At 80 °C. A solution of benzil (0.50 g, 0.000 238 mol) in absolute ethanol (1.5 mL) was prepared in an NMR tube. A solution of sodium dithionite (0.062 g, 0.000 357 mol) in water (0.5 mL) was added and shaken until the suspension, thus created, was homogeneous. The sealed tube was placed in the probe of a Varian HA-100 NMR spectrometer preheated to 80 °C, and the region from 9 to 6 ppm was scanned continuously. Within the first minute, an emission signal was observed at 8.1 ppm for the protons ortho to the carbonyl group of the benzoin product. An attempt to repeat the experiment by warming the probe gradually from 45 °C led to observation of enhanced absorptions at 6.2 (CH) and 7.4 (phenyl) ppm, but with no emission signals being recorded.

At 22 °C. The reaction was again conducted in an NMR tube by using the procedure above except that deoxygenated solvents were utilized and the scale of the reaction was reduced in an effort to obtain a more homogeneous system. Thus, benzil (0.015 g, 0.000 071 4 mol) was dissolved in absolute ethanol (1.5 mL). The solution was scanned upfield to about δ 5.4 where the ethanol solvent began to be detected. The characteristic benzil resonances were observed at δ 7.42–7.80 (6 protons) and 7.88–7.99 (4 protons). Chemical shifts were assigned by using the ^{13}C satellites of the methyl resonance for ethanol centered at δ 1.16.[31] The dithionite (0.019 g, 0.000 107 mol) dissolved in water (0.5 mL) was added whereupon a white suspension resulted. The NMR spectrum immediately showed diminished benzil resonances and a rather narrow multiplet centered at δ 7.18. Within 14 min the benzil resonances had disappeared and only the δ 7.18 resonance was detected. After 20 min the characteristic resonances of the benzoin product were just beginning to be detected. The reaction was monitored at 30, 55, and, finally, at 150 min where integration indicated an intermediate to benzoin molar ratio of 9:91.

The ^{13}C NMR spectrum was recorded at 15-min intervals over a 1-h period. Although the spectra were never totally free of either benzil starting material or benzoin product, the intermediate displayed basically a five-line spectrum with resonances at 126.8, 127.5, 128.4, 135.1, and 135.9 ppm. These compared favorably with relevant resonances of (*Z*)-1,2-bis(trimethylsiloxy)stilbene[15] at 126.8, 127.8, 129.6, 136.9, and 138.3 ppm. The resonances at 135.1 and 135.9 ppm for the intermediate diminished in intensity with time.

Examination of the Dithionite Reduction of Benzil in the ESR Probe. Initially, the paramagnetic resonance behavior of a deoxygenated solution of sodium dithionite (0.08 g, 0.000 46 mol) in water (2 mL) was examined in the flat cell at room temperature. A very intense resonance was observed for the sulfur dioxide radical anion with a spectroscopic splitting factor, *g*, of 2.0055. Next, a mixture composed of benzil (0.050 g, 0.000 238 mol), sodium dithionite (0.080 g, 0.000 46 mole), ethanol (1.5 mL), and water (0.5 mL) was placed in the cell and its ESR activity examined over a 2-h period at room temperature. No resonances other than for the sulfur dioxide radical anion were detected. TLC analysis of the reaction solution after this period revealed that reaction had gone virtually to completion. In a similar fashion, no additional resonances were observed when a fresh reaction mixture was warmed at 70 °C for 2 min.

UV Investigation of the Intermediate in the Dithionite Reduction of Benzil. Various controls including benzil, benzoin, and the supernatant of a sodium dithionite mixture were recorded at 4×10^{-5} M concentrations in ethanol–water (3:1 v/v) vs. an ethanol–water (3:1 v/v) blank. The benzil exhibited a λ_{max} = 262 nm, the benzoin λ_{max} = 251, and the dithionite exhibited essentially no absorption in the 220–360-nm range. Next, a solution of benzil (0.03 g, 0.000 14 mol) in deoxygenated ethanol (3 mL) was prepared in a septum-capped centrifuge tube. A solution of sodium di-

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[31] Kasler, F "Quantitative Analysis by NMR Spectroscopy"; Academic Press: New York, 1973; p 53.

thionite (0.03 g, 0.000 22 mol) in deoxygenated water (1 mL) was added, causing precipitation of a white solid. The mixture was shaken occasionally for 5 min before centrifugation. Then, 3.42 μL of the supernatant were added to a UV cell containing deoxygenated ethanol (2.5 mL) and water (0.75 mL) to achieve an approximate concentration of the intermediate of 4×10^{-5} M. The UV range from 220 to 360 nm was then monitored, with a fairly broad absorption with λ_{max} = 260 nm being recorded. With time and with freshly prepared samples from the original stock solution, the absorption gradually diminished and shifted to λ_{max} = 255 nm after about 80 min. No absorption between 310 and 318 nm for the (*E*)-stilbenediol[13,16] was detected. The final spectrum recorded after 80 min compared very well with that of spectrum d of Figure 1 of ref 13.

Electrochemical Investigation of the Intermediate in the Dithionite Reduction of Benzil. A solution of benzil (0.001 M) in ethanol–water (1:1 v/v) with a 0.1 M NaAc–HOAc electrolyte at pH 5[32] was prepared by dissolving benzil (0.021 g, 0.0001 mole) in ethanol (50 mL) and an aqueous solution made up of 35 mL of 0.2 M sodium acetate and 15 mL of 0.2 M acetic acid. The potential range from −1.0 to 0.0 V (Ag–AgCl) was then scanned at 50 mV s^{-1}. The (*E*)- and (*Z*)-stilbenediols were clearly distinguished (Figure 1a) with peak potentials of −0.38 and −0.28 V, respectively. Next, a solution of the dithionite intermediate identical with that described in the UV study above was prepared and centrifuged. An aliquot (0.1 mL) of the supernatant was added to the cell containing the 0.001 M benzil and the potential range scanned again. This time (Figure 1b) the peak for the Z isomer (E_p = −0.28 V) was dramatically increased.

Reduction of Benzil with Sodium Formaldehydesulfoxylate. Benzil (0.50 g, 0.002 38 mol) was dissolved in ethanol (15 mL). Sodium formaldehydesulfoxylate (2.66 g, 0.017 mol) was dissolved in 5 mL of 1.5 N HCl and added to the stirring benzil solution at room temperature. A control reaction was also run at the same time, identical with the above except that the sodium formaldehydesulfoxylate was dissolved in 5 mL of distilled water. Stirring was continued for a total of 3.5 h at room temperature, at which time the reaction mixtures were poured into 100 mL of H_2O, extracted with CH_2Cl_2, dried (Na_2SO_4), filtered, and evaporated to dryness. ^{1}H NMR analysis of the solid residues showed the control to consist solely of benzil, while the reaction mixture produced in the presence of HCl consisted of benzil (58.7%) and benzoin (41.3%).

Reduction of 4-Chlorobenzil. 4-Chlorobenzil (0.25 g, 0.001 mol) was dissolved in 7.5 mL of ethanol. Sodium formaldehydesulfoxylate (1.33 g, 0.011 mol) dissolved in 2.5 mL of 1 N HCl was added with stirring at room temperature. The reaction was monitored by TLC (silica gel with chloroform). Additional solid sodium formaldehydesulfoxylate was added in small portions at 30-min intervals over the next 4 h, and then the mixture was allowed to stir at room temperature overnight. Workup as before produced a pale yellow solid which was shown by ^{1}H NMR to consist of 4-chlorobenzoin (**2a**, 64%) and 4′-chlorobenzoin (**3a**, 36%).

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Registry No. **1a**, 22711-23-5; **1b**, 2431-00-7; **1c**, 22711-21-3; **1d**, 38469-73-7; **2a**, 71292-81-4; **2b**, 2431-02-9; **2c**, 1889-84-5; **2d**, 5230-33-1; **3a**, 39774-18-0; **3b**, 2431-23-4; **3c**, 4254-17-5; **3d**, 54551-71-2; **7**, 42788-50-1; **10a**, 84812-18-0; **10b**, 84812-19-1; **10c**, 84812-20-4; **10d**, 84812-21-5; sodium dithionite, 7775-14-6; sodium formaldehydesulfoxylate, 149-44-0.

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[32] Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. "Purification of Laboratory Chemicals"; Pergamon Press: London, 1966; p 41.

Mechanism of Oxidation of Trialkylamines by Ferricyanide in Aqueous Solution

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Rates of oxidation of triethylamine, *N*-methylpyrrolidine, and triethanolamine by aqueous ferricyanide have been determined over the range pH 3.7–13.4. Although rates were greater in the more strongly alkaline solutions, no correlation between rate and ratio of unprotonated/protonated amine was found. The oxidations were inhibited in the presence of added ferrocyanide over the entire pH range; correlations of inhibition with ferrocyanide concentration were linear, with the slopes being greater at lower pH. Two rate-determining processes, electron transfer from amine free base (predominant at high pH) and hydrogen transfer from trialkylammonium cation (predominant at intermediate and lower pH), are proposed to account for these observations. Both processes are reversible, and the slopes and intercepts of the inhibition curves may reflect the relative ease of trapping and generating, respectively, intermediates in the two different processes.

Ferricyanide has long been known to react with electron-rich organic compounds by one-electron abstraction processes,[1] and its oxidation of a variety of trialkylamines was investigated mechanistically in a series of papers by Lindsay Smith and co-workers in the 1970s.[2] The characteristics of these amine oxidations by ferricyanide were strikingly similar to those observed for aliphatic amine oxidations by chlorine dioxide (ClO_2), another one-electron oxidant, in aqueous solution.[3] A significant difference, however, was the irreversibility of the rate-determining electron abstraction step (eq 1) reported in the ferricyanide

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[2] (a) Audeh, C. A.; Lindsay Smith, J. R. *J. Chem. Soc. B* **1970**, 1280–1285. (b) Audeh, C. A.; Lindsay Smith, J. R. *Ibid.* **1971**, 1741–1744. (c) Lindsay Smith, J. R.; Mead, L. A. V. *J. Chem. Soc., Perkin Trans. 2* **1973**, 206–210. (d) Lindsay Smith, J. R.; Mead, L. A. V. *Ibid.* **1976**, 1172–1176.

[3] For a summary see: Rosenblatt, D. H.; Burrows, E. P. In "The Chemistry of Amines, Nitroso and Nitro Groups and Their Derivatives"; Patai, S., Ed.; Wiley: Chichester, England, 1982; Supplement F, pp 1086–1090, 1098–1099.