For triorganogermyl radicals we also suggest that reactivity will be nearly the same whether alkyl or aryl groups are attached to the germanium.[70] Sakurai and Mochida[52] reported in 1971 that when (1-naphthyl)phenylmethylgermyl was generated from the optically active parent germane in the presence of CCl_4 it gave optically active germyl chloride. More recently Mochida et al.[71] have studied the variation in the optical purity of the product as a function of CCl_4 concentration. Kinetic analysis[9,71] yields $k_{trap}/k_{inv} = (0.52 \pm 0.13)$ M^{-1} at 80 °C, where k_{trap} is the rate constant for reaction of the germyl radical with CCl_4 at the temperature of the experiment. If at this temperature we assume a value of 5×10^8 M^{-1} s^{-1} for k_{trap} then $k_{inv} \sim 9.6 \times 10^8$ s^{-1}. This value is somewhat less than the rate constant for the analogous silyl radical inversion at 80 °C (6.8×10^9 s^{-1}). If we assume that both inversions have the same pre-exponential factor, the barriers must differ by 1.4 kcal/mol.

(70) As support for this view we note that the rate constants for H-atom abstraction by *tert*-butoxyl from *n*-Bu_3GeH and Ph_3GeH are equal within experimental error.[6]

(71) Mochida, K.; Yamaguchi, T.; Sakurai, H., *J. Organometal. Chem.*, submitted for publication.

Acknowledgment. Thanks are due to Mr. S. E. Sugamori for his technical assistance. We also thank Dr. K. Mochida for making his unpublished results available to us.

Registry No. *n*-Bu_3GeCl, 2117-36-4; *n*-$Bu_3Ge\cdot$, 55321-84-1; *n*-$Bu_3Sn\cdot$, 20763-88-6; *n*-Bu_3GeH, 998-39-0; *n*-Bu_3SnH, 688-73-3; $C_6H_5COCOC_6H_5$, 134-81-6; $[CF_3CF_2C(O)]_2O$, 356-42-3; CH_3CH_2CHO, 123-38-6; $H_2C{=}CHC{\equiv}N$, 107-13-1; $H_2C{=}C(CH_3)C(O)CH_3$, 814-78-8; $H_2C{=}CCl_2$, 75-35-4; $H_2C{=}CHC_6H_5$, 100-42-5; *cis*-$H_2C{=}CH{-}CH{=}CHCH_3$, 1574-41-0; *trans*-$H_2C{=}CH{-}CH{=}CHCH_3$, 2004-70-8; C_6H_6, 71-43-2; $C_6H_5CH_3$, 108-88-3; CH_3I, 74-88-4; $CH_3CH_2CH_2I$, 107-08-4; $C_6H_5CH_2Br$, 100-39-0; $(CH_3)_3CBr$, 507-19-7; $CH_3CH_2CH_2Br$, 106-94-5; C_6H_5Br, 108-86-1; CCl_4, 56-23-5; $C_6H_5CH_2Cl$, 100-44-7; $(CH_3)_3CCl$, 507-20-0; duroquinone, 527-17-3; fluorenone, 486-25-9; cyclohexanone, 108-94-1; 1,3-cyclooctadiene, 1700-10-3; β-pinene, 127-91-3.

Supplementary Material Available: Tables giving detailed kinetic data for the reactions studied (33 pages). Ordering information is given on any current masthead page.

Solid-State Formation of Quinhydrones from Their Components. Use of Solid–Solid Reactions To Prepare Compounds Not Accessible from Solution

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Abstract: Selective molecular mobility provided by working with crystalline solids has been employed to prepare unsymmetrically substituted quinhydrones too unstable with respect to self-oxidation–reduction to be prepared by crystallization from solution. Reaction is carried out by grinding the solid components together with a mortar and pestle. Examination of the products with differential scanning calorimetry, X-ray powder photography, and Fourier transform infrared spectroscopy shows that the complexation reaction goes to completion under conditions in which no detectible redox reaction has occurred. The products are shown by X-ray powder photography to be formed in a microcrystalline state. The quinones employed for complex formation include 1,4-benzoquinone, its methyl and phenyl derivatives, 2,5-dimethyl-1,4-benzoquinone, and naphthoquinone. The hydroquinones are those obtained from this set of quinones by reduction. This method allows the formation of isomeric pairs of unsymmetrically substituted complexes such as benzoquinone–naphthohydroquinone and naphthoquinone–benzohydroquinone. Such isomeric complexes differ in color and have different infrared spectra and X-ray powder patterns. In cases where it is possible to prepare the complex by crystallization from solution its color, infrared spectrum, crystal structure, and other properties are identical with those of the same complex obtained by grinding the solid components together. Although the complexes formed in this way generally contain the quinone and hydroquinone in a ratio of 1:1, the complex of 2,5-dimethyl-1,4-benzoquinone with hydroquinone is composed of two hydroquinone molecules for each quinone and that of 2-methyl-1,4-benzoquinone with hydroquinone has a somewhat variable ratio of 1:1.5 to 1:2. In each of these cases the same complex is obtained when prepared by crystallization from solution; no 1:1 complex has been obtained from these pairs of reactants.

Unsymmetrically substituted quinhydrones have long been known to undergo a redox exchange reaction rapidly in solution but much less so in the solid state. For example, the unsymmetrically deuterium-labeled compound **1** and its redox isomer **2**,[1] the ^{14}C-labeled duroquinone–hydroduroquinone pair **3** and **4**,[2] and the phenylhydroquinone–*p*-chlorophenylbenzoquinone **5** and its redox isomer **6**[3] have been prepared as solids, each essentially free from the other, and found to be stable in the crystalline state at room temperature. Although the deuterioquinhydrones **1** and **2** had been reported[1c] to undergo slow interconversion as powders when heated in the temperature range 107–120 °C, the phenylquinhydrones **5** and **6** were not interconverted even after several

(1) (a) Gragerov, I. P.; Miklukhin, G. P. *Dokl. Akad. Nauk SSSR* **1948**, *62*, 79–81. (b) Gragerov, I. P.; Miklukhin, G. P. *Zh. Fiz. Khim.* **1950**, *24*, 582–588. (c) Brodskii, A. I.; Gragerov, I. P.; Pisarzhevskii, L. V. *Dokl. Akad. Nauk SSSR* **1951**, *79*, 277–279.

(2) (a) Bothner-by, A. A. *J. Am. Chem. Soc.* **1951**, *73*, 4228–4230. (b) *Ibid.* **1953**, *75*, 728–730.

(3) (a) Desiraju, G. R.; Curtin, D. Y.; Paul, I. C. *J. Org. Chem.* **1977**, *42*, 4071–4075. (b) Desiraju, G. R.; Curtin, D. Y.; Paul, I. C. *J. Am. Chem. Soc.* **1977**, *99*, 6148. (c) Desiraju, G. R.; Curtin, D. Y.; Paul I. C. *Mol. Cryst. Liq. Cryst.* **1979**, *52*, 259–265. (d) Curtin, D. Y.; Paul, I. C. *Chem. Rev.* **1981**, *81*, 525–541.

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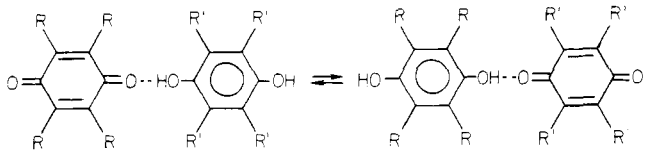

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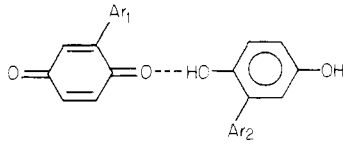


5, 6

1, **2**, R = H, R′ = D; **3**, **4**, R = CH_3, R′ = $^{14}CH_3$; **5**, Ar_1 = C_6H_5, Ar_2 = *p*-ClC_6H_4; **6**, Ar_1 = *p*-ClC_6H_4, Ar_2 = C_6H_5

hours of heating at over 142 °C, and in fact, conditions were not found whereby they could be made to isomerize in the solid state.[3a]

Since the equilibria between the members of each of these pairs of isomers would be expected to be effectively thermodynamically balanced, it was hoped that the rate of equilibration in the solid might be increased if some quinhydrones were chosen having more one-sided equilibria, as judged from their behavior in solution.[4] However, this presented a synthetic problem since attempts to prepare the unstable member of such a pair of quinhydrones by crystallization from a solvent lead to products whose formation is accompanied by redox hydrogen exchange.[5]

A possible exit from this dilemma was suggested by the work of Rastogi and others,[6,7] who had studied complex formation induced by grinding the reactants together. In particular the formation of quinhydrone from 1,4-benzoquinone and 1,4-hydroquinone had been referred to but no details of the study of this reaction were given.[6a] However, Slifken and Walmsley[8] had raised some doubt about the general utility of the method; they found that a slightly modified method of grinding components together with a mortar and pestle failed to give complete reaction when hydroquinone was ground with any of a number of chlorinated quinones. Furthermore, in none of the previous studies was there a preparation of the unstable complex of an unsymmetrically substituted pair.

The questions to be answered, then, were (1) could the formation of the complexes by mechanical mixing of the components, in the case of substituted quinones and hydroquinones, be induced to go to completion and (2) could conditions be found which led to complex formation but did not allow the redox rearrangement of the first-formed complex to the stable isomer? In addition there was a need to find analytical methods which would give adequate information about the chemical composition and crystallinity of such solid complexes.

This paper describes the preparation of isomeric pairs of complexes by mechanical mixing and explores some of the factors affecting such "solid–solid" reactions.

Experimental Section[9]

Sources and Purification of the Quinones and Hydroquinones. 1,4-Benzoquinone (**7a**), mp 115–116 °C (high-boiling petroleum ether), 2-methylbenzoquinone (**7b**), mp 69–70 °C, 1,4-hydroquinone (**8a**), mp 171–172 °C, 2-methylhydroquinone (**8b**), mp 126–127 °C, and 1,4-naphthoquinone (**9**), mp 125–126 °C (diethyl ether, Norit), were purchased from the Aldrich Chemical Co. and purified by crystallization from the solvent indicated followed by sublimation. 2-Phenyl-1,4-hydroquinone (**8c**), mp 100–102 °C (chloroform), and 2,5-dimethyl-1,4-benzoquinone (**11**), mp 125–126 °C (sublimed), were purchased from the Eastman Kodak Co. and purified as indicated. 1,4-Hydronaphthoquinone (**10**), mp 195–196 °C, was prepared from quinone **9** by reduction with aqueous sodium hydrosulfite[10] and purified by sublimation. 2-Phenyl-1,4-benzoquinone (**7c**), mp 111–112 °C, was prepared by reaction of benzenediazonium chloride with 1,4-benzoquinone[11] and purified by sublimation at 90 °C and 0.05 torr. 2,5-Dimethyl-1,4-hydroquinone (**12**), mp 217–218 °C, was prepared by reduction of 2,5-dimethyl-1,4-benzoquinone (**11**) with sodium hydrosulfite analogous to that of 1,4-dihydronaphthoquinone.[10]

Preparation of Quinhydrones by Grinding. An agate mortar and pestle were employed to grind the appropriate amounts (typically 10^{-3} mol) of the quinone and hydroquinone weighed to ±0.1 mg until there was no further visible change and then for an additional 5 min. In no case was any liquid detectible.

Structures of quinone, hydroquinone, product melting point (°C), time of grinding (min), color of quinhydrone, and infrared absorption peaks (cm^{-1}), which disappeared during reaction, were as follows: 1,4-benzoquinone, 1,4-hydroquinone, 168–170, 15–20, black-gold, 1658, 1645, 1311, 1306, 1242, 1190, 898, 825; 2-methyl-1,4-benzoquinone, 2-methyl-1,4-hydroquinone, 101–102, 15–20, black, 1660, 1500, 1280, 1230, 1096, 927, 825, 818; 2-phenyl-1,4-benzoquinone, 2-phenyl-1,4-hydroquinone, 177–178, 20–25, reddish blue, 3533, 1657, 1512, 1343, 936, 912, 842, 800; 1,4-naphthoquinone, 1,4-naphthohydroquinone, 164–166, 20–25, blue, 1661, 1604, 1264, 864, 825, 774; 1,4-benzoquinone, 2-methyl-1,4-hydroquinone, –,[9b] 15–20, blackish-violet, 1072, 930, 742; 1,4-benzoquinone, 2,5-dimethyl-1,4-hydroquinone, –,[9b] 15–20, blackish violet, 1658, 1645, 1311, 1306, 1268, 942, 898; 1,4-naphthoquinone, 1,4-hydroquinone, 124–125, 20–25, reddish blue, 1660, 1116, 1008, 998, 986, 864; 1,4-naphthohydroquinone, 1,4-benzoquinone, –,[9b] 20–25, blue-black, 1311, 1072, 898; 1,4-naphthoquinone, phenyl-1,4-hydroquinone, 130–131, 20–25, reddish blue, 3533, 1092, 997, 800; 1,4-naphthohydroquinone, phenyl-1,4-benzoquinone, –,[9b] 20–25, blue-black, 1445, 936, 908, 800.

Fourier transform infrared spectra were measured with Nujol mulls. A doublet at 1645 and 1655 (lit.[8] (KBr disk) 1648–1663) in the carbonyl stretching region of benzoquinone **7a** was replaced by a sharp maximum at 1630 cm^{-1} in both monoclinic and triclinic quinhydrone (**7a**/**8a**) (lit.[8] (KBr disk) 1634 cm^{-1}). In its complexes with other hydroquinones quinone **7a** showed multiple absorption in the carbonyl region as follows: naphthalenediol **10** 1632 (w), 1648 (s), 1661 (w); methylhydroquinone **8b** 1636 (sh 1658, 1678); dimethylhydroquinone **12** 1635 (s), 1666 (w). The complex of phenylquinone **7c** (C=O 1658, 1645, sh 1630) with naphthohydroquinone **10** had the C=O absorption as an unresolved multiplet at 1629–1660 cm^{-1}. The complex of naphthoquinone **9** (1660 broad) with hydroquinone **8a** showed C=O at 1646 (sharp) and that with phenylhydroquinone **8c** at 1645 (sharp). The O–H stretch region of each of the hydroquinones was a very intense broad peak centered between 3200 and 3300 cm^{-1}. In the 1:1 complexes it was markedly triangular in shape and centered at 3200–3300 cm^{-1}. Other peaks showing minimum interference of absorptions of the starting materials with those of the complexes are given above.

1:2 Complex of 2-Methyl-1,4-benzoquinone (7b) with 1,4-Hydroquinone (8a). Attempts to prepare the 1:1 complex by crystallization by a previously described method[3a] gave only the reddish brown complex with **7b** and **8a** in a ratio varying from 1:1.5 to 1:2 mp 140–141; FT-IR (Nujol mull) 3380 (s), 3240 (broad), 1630 (s) cm^{-1} (absorptions at 1660, 1280, 1190, 927, and 795 disappeared during grinding); ^1H NMR (Me_2SO-d_6) δ 8.5 (s, 4 H), 6.70 (m, 3 H), 6.57 (s, 8 H), 1.95, (d, 3 H); ^1H (quinoid)/^1H(aromatic) 0.42, 0.41 (theoretical for a ratio of 1:2 0.375); ^1H(methyl)/^1H(hydroxyl) 0.75, 0.69 (theoretical for a ratio of 1:2 0.75).

(4) (a) Conant, J. B.; Fieser, L. F. *J. Am. Chem. Soc.* **1923**, *45*, 2194–2218. (b) Conant, J. B.; Fieser, L. F. *Ibid.* **1924**, *46*, 1858–1881. (c) Hunter, W. H.; Kvalnes, D. E. *Ibid.* **1932**, *54*, 2869–2880. (d) Kvalnes, D. E. *Ibid.* **1934**, *56*, 668–670. (e) Kvalnes, D. E. *Ibid.* **1934**, *56*, 670–672. (f) Kvalnes, D. E. *Ibid.* **1934**, *56*, 2478–2481.

(5) Urban, R. *Monatsh. Chem.* **1907**, *28*, 299–318.

(6) (a) Rastogi, R. P. *J. Sci. Ind. Res.* **1970**, *29*, 177–180. (b) Rastogi, R. P.; Singh, N. B. *J. Phys. Chem.* **1966**, *70*, 3315–3324. (c) Rastogi, R. P.; Bassi, P. S.; Chadha, S. L. *Ibid.* **1963**, *67*, 2569–2573. (d) Rastogi, R. P.; Singh, N. B.; *J. Phys. Chem.* **1968**, *72*, 4446–4449.

(7) The earliest report of the preparation of a quinhydrone by grinding the solid components together seems to be that of Ling and Baker: Ling, A. R.; Baker, J. L. *J. Chem. Soc.* **1893**, *63*, 1314–1327. Other more recent references to solid–solid reactions are the following: Sato, H.; Yasuniwa, T. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 368–372. Ramachandran, S.; Baradarajan, A.; Satyanarayana, M. *Can. J. Chem. Eng.* **1974**, 364–368.

(8) Slifkin, M. A.; Walmsley, R. H. *Spectrochim. Acta, Part A* **1970**, *26A*, 1237–1242.

(9) (a) Fourier transform infrared spectra were obtained with a Nicolet 7000 FT-IR spectrophotometer, and differential calorimetry scans were recorded with a DuPont 900 Thermal Analyzer. (b) Where no melting point is quoted the complex is thermally unstable.

(10) Fieser, L. F.; Tishler, M.; Wendler, N. L. *J. Am. Chem. Soc.* **1940**, *62*, 2864–2866.

(11) Brassard, P.; L'Ecuyer, P. *Can. J. Chem.* **1958**, *36*, 700–708.

Grinding of the quinone (122.1 mg, 1×10^{-3} mol) with hydroquinone (220.2 mg, 2×10^{-3} mol) gave a complex whose FT-IR was identical with that found by crystallization from a solvent as described above. The DSC showed a single sharp endotherm at 140 °C.

Grinding of quinone and hydroquinone in a molar ratio of 1:1 gave a complex whose DSC showed two endotherms corresponding to the excess quinone (70 °C) and the 1:2 complex above (140–141 °C). The FT-IR of this preparation showed the expected absorption peaks of the 1:2 complex above with additional peaks due to the excess ketone.

1:2 Complex of 2,5-Dimethyl-1,4-benzoquinone (11) with 1,4-Hydroquinone (8a). Attempts to prepare the 1:1 complex by crystallization[3a] or gel diffusion[3b] gave a reddish brown complex containing the quinone and hydroquinone in a ratio of 1:2: mp 166–168 °C; FT-IR (Nujol mull) 3150 (broad) 3380 (s), 1670 (s), 1620 (s) cm^{-1} (absorptions at 1663, 1640, 1292, 1190, 927, and 795 disappeared on grinding); ^1H NMR (Me_2SO-d_6) δ 8.55 (s, 4 H), 6.75 (m, 2 H), 6.58 (s, 8 H), 1.95 (d, 6 H); ^1H(quinoid)/^1H(aromatic) 0.27, 0.23 (theoretical for 1:2 0.25); ^1H(hydroxyl)/^1H(methyl) 0.65, 0.67 (theoretical for 1:2 0.67). Preparation of the complex by grinding the quinone (136.1 mg, 1×10^{-3} mol) with the hydroquinone (220.1 mg, 2×10^{-3} mol) gave a complex whose FT-IR was identical with that prepared by the methods above. DSC showed a single endotherm characteristic of the complex. When the quinone and hydroquinone were ground in a ratio of 1:1, the FT-IR showed the same peaks as the 1:2 complex above with additional peaks characteristic of excess ketone. The DSC of the ground 1:1 mixture showed an endotherm due to quinone (115 °C) and one due to the 1:2 complex (166–168 °C).

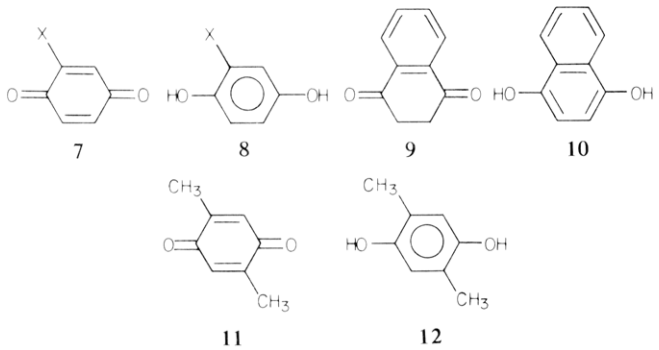
Reactions of Quinones with Hydroquinones in Capillaries. The quinone and hydroquinone reactants were thoroughly (5 min) ground (separately) in a mortar and pestle after which the quinone was inserted into one end and the hydroquinone into the other of a KIMAX-51 capillary tube (i.d. 1.5, o.d. 1.8 mm, length 100 mm) and the two solids pushed toward each other with small glass rods until they met and a sharp interface was formed. The capillary was allowed to stand on a desk top at a laboratory temperature of 22–25 °C. No liquid was observed in the capillaries. Since only gross differences in reactivity were considered significant, we did not attempt to make a quantitative estimate of reaction rates.

Differential Scanning Calorimetry. DSC traces were obtained from samples sealed in aluminum cups heated at a rate of 10 °C/min, scanning at 20 °C/in., and sensitivity of 0.2.

X-ray Powder Photography. Powder photographs were taken with a Debye-Sherrer camera (Cu Kα radiation) manufactured by the Charles Supper Co.

Results and Discussion

A quinone (**7**, **9**, or **11**) and a hydroquinone (**8**, **10**, or **12**) in equimolar amounts were ground together with an agate mortar and pestle. In each case the color of the mixture, initially light



yellow, darkened quickly as reaction occurred and the deeply colored π complex appeared. In none of the examples studied was softening or formation of a liquid phase observed. Grinding was continued until no further color change was observed (10 to 20 min) and for an additional 5 min. The product from unsubstituted quinone **7a** and hydroquinone **8a** was shown to be microcrystalline by X-ray powder photography and, moreover, the powder photograph was that to be expected from a mixture of monoclinic[12c] and triclinic[12b] forms of quinhydrone prepared from solution. Similarly the powder photographs of the stable quinhydrones, naphthoquinone **9**:hydroquinone **8a** and naphthoquinone **9**:hydroquinone **8c**, prepared by solid–solid reaction, agreed with

(12) (a) Matsuda, H.; Osaki, K.; Nitta, I. *Bull. Chem. Soc. Jpn.* **1958**, *31*, 611. (b) Sakurai, T. *Acta Crystallogr.* **1965**, *19*, 320–330. (c) Sakurai, T. *Acta Crystallogr., Sect. B* **1968**, *B24*, 403–412.

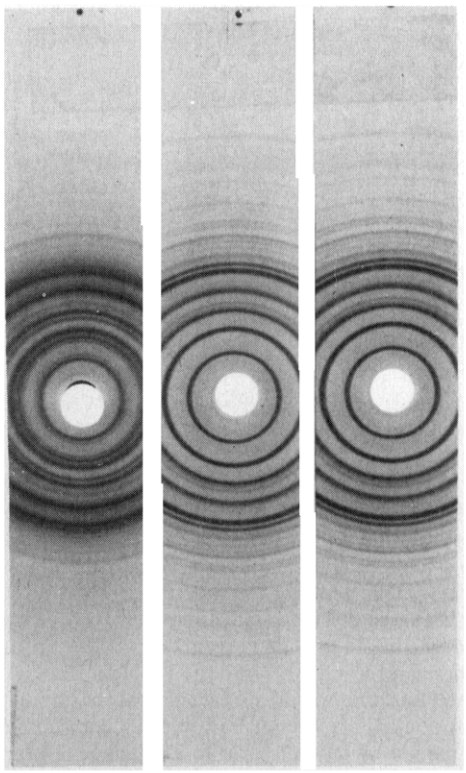


Figure 1. X-ray powder photography of (a) (left-hand photograph) the unstable quinhydrone from phenylquinone **7c** and naphthohydroquinone **10** prepared by grinding the components together in a mortar and pestle, (b) (middle photograph) the stable complex from naphthoquinone **9** and phenylhydroquinone **8c** prepared by grinding the components together, and (c) (right-hand photograph) the complex from **9** and **8c** prepared by crystallization from solution.

the powder photographs of the same quinhydrones prepared from solution (see Figure 1). Most interesting were the reactions of benzoquinone **7a** with methylhydroquinone **8b** and of benzoquinone **7a** or phenylquinone **7c** with naphthohydroquinone **10**. These are reactions whose products would be expected to undergo rapid redox isomerization in solution.[3-5] There were obtained from the solid–solid reactions crystalline products whose X-ray powder photographs were distinctly different from those of the isomeric pairs **7b** + **8a**, **9** + **8a**, or **9** + **8c** which would have been formed if the redox reaction had accompanied formation of the complex. In each case certain powder lines present in the separate photographs of the starting quinone and hydroquinone disappeared during grinding and other lines not present in the starting materials appeared in the ground product.

Differential scanning calorimetry (DSC) provided a sensitive method of following the progress of the reaction with the advantage that the samples required no special preparation for analysis (such as grinding in paraffin oil). As reaction took place DSC showed progressively smaller melting endotherms associated with the starting materials, and at the end of the reaction there was the single endotherm characteristic of the product (see Figure 2). The method was shown to be easily capable of detecting less than 1% of the starting quinone in an artificial mixture with a quinhydrone.

The most informative method of following the reaction was Fourier transform infrared spectroscopy (FT-IR). Slifkin and Walmsley[8] had previously examined the IR spectra of KBr disks of benzoquinone **7a**, hydroquinone **8a**, as well as their complex, quinhydrone, and some of their chlorinated derivatives and pointed out that IR spectra could be used to distinguish between the complexes and their precursors. The carbonyl stretching frequency, although complicated by the presence of multiple absorptions due to Fermi resonance, shifts to lower frequency on formation of the hydrogen-bonded complex. We have found similar shifts to occur in all of the complexes studied here. Although their breadth sometimes led to partial-overlap of the carbonyl absorptions of starting quinone with those of the complex,

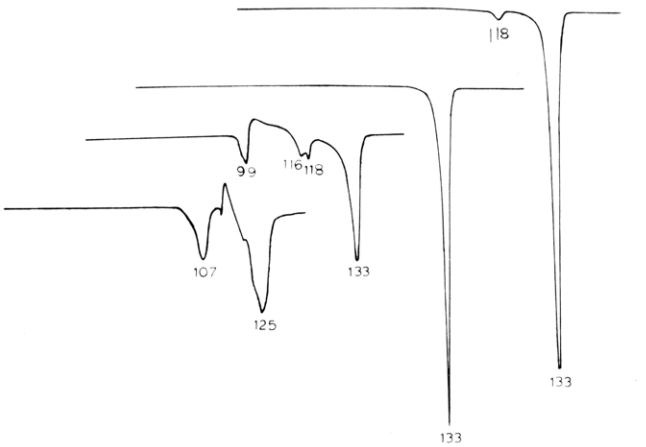


Figure 2. Differential scanning calorimeter traces showing the progress of the reaction of quinhydrone formation by grinding together **8c** and **9**. (a lower curve) An unground mixture of the starting materials, (b, lower-middle curve) reaction at an intermediate stage—note the endotherm at 133 °C due to the complex that has been formed, (c, upper-middle curve) completed reaction, and (d, upper curve) an artificial mixture of the quinhydrone complex to which has been added 1% of the naphthoquinone in order to test the sensitivity of the method.

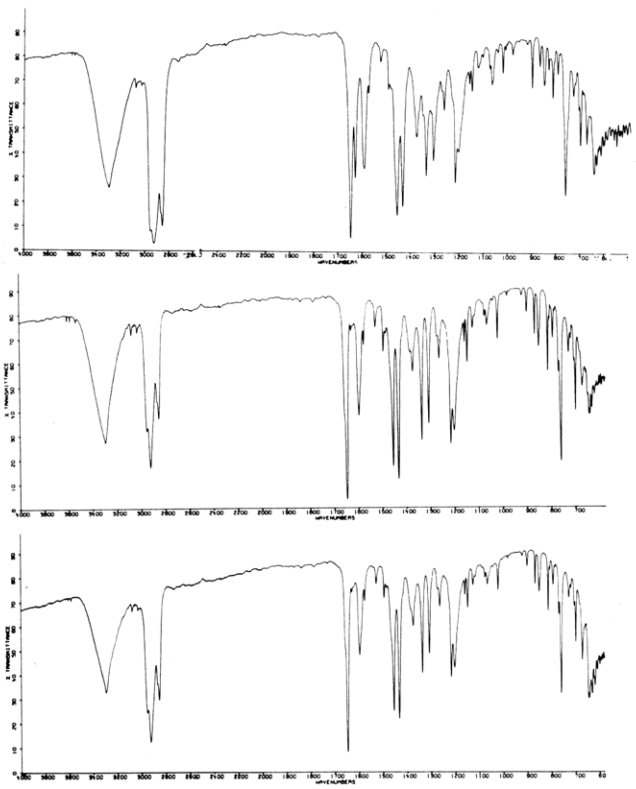


Figure 3. FT-IR spectra of Nujol mulls of (a, top) the unstable quinhydrone from **7c** and **10** prepared by grinding the components together (note that the splitting of the C=O stretching frequency particularly evident in the spectrum of 1,4-benzoquinone (ref 8) **is** evident also in the complex (1629–1660 cm^{-1}), (b, middle) the stable quinhydrone from **9** and **8c**, and (c) the stable quinhydrone prepared from **9** and **8c** by crystallization from solution. The C=O stretching absorption gives rise to a singlet in the complex as it does in 1,4-naphthoquinone alone.

the infrared spectra of solid quinhydrone complexes prepared in Nujol mull showed both certain frequencies characteristic of the starting materials that were absent in the product and the reverse. Spectra of the stable quinhydrones prepared by grinding were identical with those prepared by crystallization from a solvent (see Figure 3).[13] The unstable quinhydrones also gave spectra quite

(13) This is true of the 1:2 as well as the 1:1 complexes.

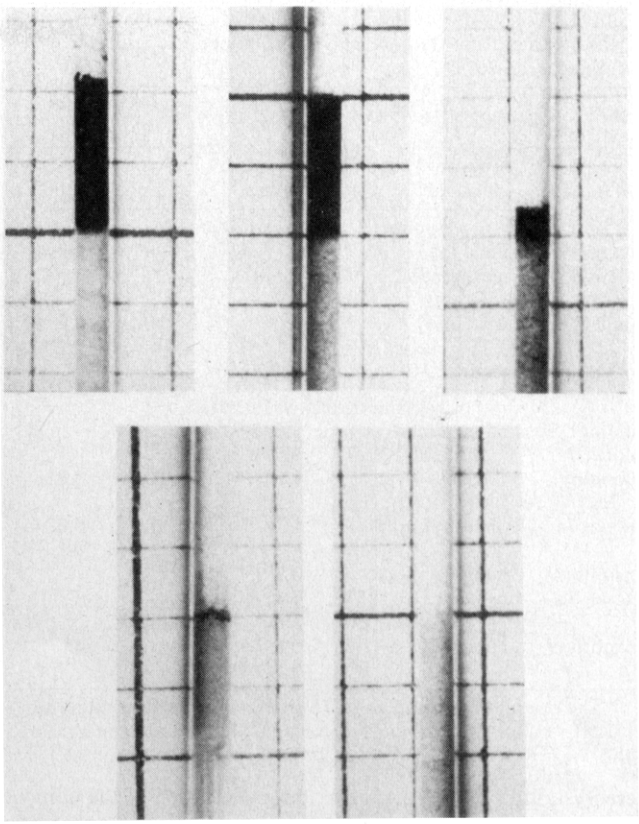


Figure 4. Capillary tubes containing quinone and hydroquinone. In each case the quinone has been placed in the lower part of the capillary and the hydroquinone in the upper with the initial interface near the middle. The markings on the scale are 1/10 in. apart. Upper left: 1,4-Benzoquinone (**7a**) (lower part of tube) and 1,4-hydroquinone (**8a**) after 7 days. The dark region starting from the heavy line in the middle of the picture is due to complex formation. The front is moving primarily through the hydroquinone layer toward the top of the photograph. Upper middle: methylquinone **7b** and hydroquinone **8a** after 18 days. Upper right: methylquinone **7b** and methylhydroquinone **8b** after 39 days. Lower left: phenylbenzoquinone **7c** and naphthohydroquinone **10** after 43 days. Lower right: dimethylbenzoquinone **11** and dimethylhydroquinone **12** after 18 days—after 1 month there was still no change.

different from those of the stable redox isomers, showing that no significant hydrogen transfer had been induced by the original grinding process of the synthesis or even the grinding in paraffin oil associated with preparation of the mull. However, when samples of the unstable quinhydrone were allowed to stand suspended in paraffin oil they showed the appearance of absorption due to formation of the more stable redox isomer, and in certain cases even when the FT-IR spectra were taken to higher resolution by use of an increased number of scans there was evidence of a small amount of conversion of the unstable to the stable quinhydrone.

Further information about the "solid–solid" reaction was obtained by a method that had been employed by Rastogi and his associates[6] in the study of the formation of hydrocarbon picrates and other π complexes. The quinone and hydroquinone reactants were introduced into opposite ends of open glass capillary tubes and pushed toward each other until they met with formation of a solid–solid front. The capillary was allowed to stand for a period of days and the frontal migration observed (Figure 4). The characteristic color of a π complex appeared in a thin band at the interface, and the colored zone spread along the capillary in both directions but chiefly into the hydroquinone layer. When the colored section from the reaction of benzoquinone **7a** and hydroquinone **8a** was cut out and subjected to FT-IR analysis it was found to give a spectrum consistent with that of the formation of quinhydrone but with a substantial amount of unreacted hydroquinone. Thus the colored bands appeared to contain the quinhydrone reaction product distributed on the surfaces of mi-

Table I. Progression of the Reaction Fronts on Formation of Quinhydrones from Quinone and Hydroquinone Powders in Contact at 20–25 °C

substituents on				vapor pressure (μm of Hg)	
quinone	hydroquinone	time, days	distance, mm	quinone	hydroquinone
		Symmetrically Substituted			
none, **7a**	none, **8a**	7	4.75, 4.8	98	0.018
methyl, **7b**	methyl, **8b**	7	1.1, 1.3		
		60	1.2		
dimethyl, **11**	dimethyl, **12**	7	0.0	10	0.0045
naphth, **9**	naphth, **10**	7	0.4		
		Unsymmetrically Substituted			
methyl, **7b**	none, **8a**[a]	7	3.6, 2.7		
none, **7a**	methyl, **8b**	7	1.5, 2.1		
dimethyl, **11**	none,[b] **8a**	7	1.0	10	0.018
none, **7a**	dimethyl, **12**	7	1.1	98	0.0045
naphth, **9**	none, **8a**[c]	7	0.2		
none, **7a**	naphth, **10**	7	2.1		
		60	2.8		
naphth, **9**	phenyl, **8c**	7	0.3		
		60	0.8		

[a] The product is a complex of **7b** and **8a** in a ratio varying from 1:1.5 to 1:2. [b] The product is a complex of **11** and **8a** in a ratio of 1:2. [c] Reference 18.

crocrystallites of hydroquinone, but penetration of the quinone into the interior of the hydroquinone crystallites was apparently incomplete in agreement with the previous suggestion[6a] that at least two kinds of diffusion processes with different rates are involved in reactions of this type. One, the diffusion of one reactant through the space between (or on the surfaces of) microcrystallites of the other, is relatively rapid and the second, the penetration of the molecules of one reactant into the interior of crystallites of the other, slower.

The observation that in capillaries the quinone seemed to move to the hydroquinone side of the interface more rapidly than the reverse suggested that, as had been given consideration in previous studies of picrate formation, there might be a correlation of reaction rate with vapor pressures of the reactants. Approximate distances of frontal migration are summarized in Table I. It has been well-known that quinones are, in general, more volatile than are the corresponding hydroquinones, and vapor pressures of a few relevant compounds had been determined by Coolidge and Coolidge.[14] These data are included in Table I.

Although it appears that a high vapor pressure is advantageous for high reactivity, it is clear that, as had been concluded by previous investigators in their studies of picrate formation, volatility is not the only factor affecting the rate. For example, methylquinone **7b** and methylhydroquinone **8b** showed only very slow formation of a colored layer whereas methylquinone **7b** reacted relatively rapidly with the unsubstituted hydroquinone **8a** and also the unsubstituted quinone **7a** reacted readily with methylhydroquinone **8b** (Figure 4).

A major point of interest is the effect of substitution of methyl groups on the quinone reactant on the nature of the product of the quinone–hydroquinone complexation reaction. Thus, although the solid–solid reaction of benzoquinone **7a** with 2,5-dimethylhydroquinone (**12**) gives the expected 1:1 complex, the corresponding reaction of 2,5-dimethyl-1,4-benzoquinone (**11**) with unsubstituted 1,4-hydroquinone (**8a**) gives a 1:2 complex but not the 1:1 quinhydrone. The same 1:2 complex was obtained whether complex formation was carried out as a solid–solid reaction or by crystallization from a solvent. When a 1:1 ratio of starting materials is employed, a mixture of 1:2 complex and unused ketone is formed as is apparent from the DSC traces and FT-IR spectrum. If on the other hand the correct 1:2 ratio is employed, then the product of the solid–solid reaction is the same 1:2 complex as is obtained by crystallization from a solvent as shown by DSC and FT-IR measurements. Similarly, although reaction of the unsubstituted quinone **7a** with 2-methyl-1,4-hydroquinone (**8b**) proceeds normally to give the expected 1:1 complex, the corresponding reaction of 2-methyl-1,4-benzoquinone (**7b**) with unsubstituted 1,4-hydroquinone (**8a**) gives not a 1:1 complex but a complex with methylquinone and unsubstituted hydroquinone in a ratio ranging from 1:1.5 to 1:2. It is clear then that control of the product of these solid–solid reactions is maintained by subtle crystal forces and cannot be overridden by manipulation of the ratio of starting materials.

The dimethylquinone **11** showed no visible solid–solid reaction with dimethylhydroquinone **12** (Figure 4) even after 1 month, and no complex was formed by grinding the components together; the preparation from solution of a colored complex of these components has been found to give only a 2:1 complex and not the 1:1 quinhydrone.[15]

It will be noted that in all three cases where a 1:2 complex has been found one or two methyl groups have been substituted on the quinone ring.

Studies of the kinetics of reactions of picric acid with certain aromatic hydrocarbons,[6c] naphthols,[6b] and 2-naphthylamine[6d] led Rastogi and his associates to the conclusion that in these reactions there are important contributions from surface diffusion of the more labile reaction component on the surfaces of the other and penetration into the interior of the crystalline particle by vacancy and defect mechanisms. The present results are consistent with this conclusion.

We can supply little insight into the details of the process whereby solid quinone and solid hydroquinone can so readily interpenetrate to form microcrystallites of the quinhydrone complex; the mechanism is undoubtedly complicated. It is of interest at least to examine the structural change required for this reaction. The structures of only a few hydroquinones have been determined. Hydroquinone **8a** has long been known to exist in three crystalline forms and the structures of all three are known.[16] Naphthohydroquinone has been found to crystallize in a relatively simple structure made up of hydrogen-bonded chains.[17] These structures have in common extensive hydrogen bonding of the constituent molecules to form chains or rings which must be completely dismantled if a quinhydrone is to be formed. The structures of monoclinic and triclinic quinhydrone,[12] the 1:1 complex of naphthoquinone with hydroquinone,[18] and the symmetrically substituted phenyl- and *p*-chlorophenylquinhydrones[3c] have been reported and have the common feature that there are chains of alternating hydroquinone and quinone molecules linked with hydrogen bonds; adjacent chains are held together by π complexing. There seems to be no possible transition from the parent compounds to the complex which does not involve a complete repacking of the crystal and a disordered intermediate state. It will be noted that the solid–solid formation of the unsubstituted quinhydrone gives both the monoclinic and triclinic forms as does crystallization from a solvent.

An estimate of the order of magnitude of the radii of the particles involved in these reactions has been made by placing on a microscope slide a suspension in mineral oil of the hydroquinone ground in the usual way. With an adjacent Stage Micrometer calibrated with 0.01-mm markings under 100× magnification it can be seen that the hydroquinone particles are not more than 1 μ (10000 Å) in diameter. Another estimate which gives a similar answer comes from the fact that the samples of quinhydrones

(14) Coolidge, A. S.; Coolidge, M. S. *J. Am. Chem. Soc.* **1927**, *49*, 100–105.

(15) Patil, A. O.; Wilson, S. R.; Curtin, D. Y.; Paul, I. C. *J. Chem. Soc., Perkin Trans. 2*, in press.

(16) (a) Wallwork, S. C.; Powell, H. M. *J. Chem. Soc., Perkin Trans. 2* **1980**, 641–646. (b) Lindeman, S. V.; Shklover, V. E.; Struchkov, Yu. T. *Cryst. Struct. Commun.* **1981**, 10, 1173–1179. (c) Maartmann-Moe, K. *Acta Crystallogr.* **1966**, *21*, 979–982.

(17) Gaultier, J.; Hauw, C. *Acta Crystallogr.* **1967**, *23*, 1016–1020.

(18) Thozet, A.; Gaultier, J *Acta Crystallogr., Sect. B* **1977**, *B33*, 1052–1057.

formed by grinding gave high-quality X-ray powder photographs without further treatment. It has been pointed out that the optimal particle size for powder photography is 10^3–10^5 Å.[19]

The reaction may involve features of certain gas–solid reactions which have been studied[20]—reaction at the surface of a crystalline particle leading to disruption of the structure as product is formed and then diffusion through the partially disordered region by the penetrating reagent. A preliminary examination of the reaction of single crystals of the α form of hydroquinone showed rapid and rather uniform surface attack by the vapor of 1,4-benzoquinone. When the quinone was removed the color of the complex disappeared in a few minutes leaving somewhat pitted surfaces. There was no evidence of anisotropic attack, but with the large number of molecular orientations in this structure[16a] (with 54 molecules per unit cell) this is not surprising. Attempts to find other more suitable crystals with a hydroquinone structure have thus far been unsuccesful.

Conclusion

It has been demonstrated that in the formation of quinhydrones by mixing the solid quinone and hydroquinone reactants, the solids have sufficient mobility to react completely to form a new product but not so much mobility that there is rearrangement of that product to its more stable isomer by a hydrogen-transfer reaction. This example of the use of the solid state to provide restricted (and hence selective) molecular mobility illustrates one of the more promising areas of solid-state chemistry with (among others) potential value for applications in stability studies of herbicides, insecticides, and drug products.[21] Studies of the isomerization in the solid state of the unstable quinhydrones made available by this method to the more stable isomers by hydrogen transfer will be described in a subsequent paper.

Acknowledgment. We are indebted to the National Science Foundation for support of this work.

Registry No. 7a, 106-51-4; **7a·8a** (1:1 complex), 106-34-3; **7a·8b** (1:1 complex), 55836-33-4; **7a·10** (1:1 complex), 87970-33-0; **7a·12** (1:1 complex), 87970-32-9; **7b·8a** (1:2 complex), 87970-36-3; **7b·8b** (1:1 complex), 87970-31-8; **7c**, 363-03-1; **7c·8c** (1:1 complex), 41758-38-7; **7c·10** (1:1 complex), 87970-35-2; **8a·9** (1:1 complex), 60706-28-7; **8a·11** (2:1 complex), 87970-37-4; **8c·9** (1:1 complex), 87970-34-1; **9**, 130-15-4; **9·10** (1:1 complex), 21414-85-7; **10**, 571-60-8; **11**, 137-18-8; **12**, 615-90-7; benzenediazonium chloride, 100-34-5.

(19) Brown, C. J. "X-Ray Diffraction of Polycrystalline Materials"; Peiser, H. S., Rooksby, H. P., Wilson, A. J. C., Eds.; Reinhold Publishing Corp.: New York, 1960.
(20) Paul, I. C.; Curtin, D. Y. *Science* **1975**, *187*, 19–26.
(21) Byrn, S. R. "Chemistry of Drugs"; Academic Press: New York, 1983; pp 1–368. Byrn, S. R. *J. Pharm. Sci.* **1976**, *65*, 1–22.

NOC Approach to Spiroketals. A Total Synthesis of (±)-Talaromycin B

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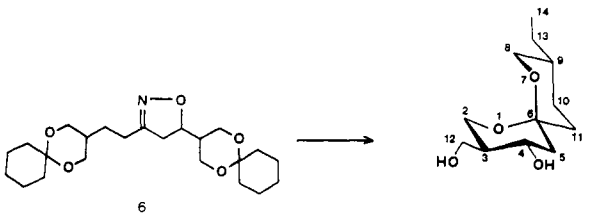
Abstract: A total synthesis of the unqiue spiroketal natural product talaromycin B (**1**) is reported. This molecule, produced in nature by the toxicogenic fungus *Talaromyces stipitatus*, was constructed in the laboratory from the isoxazoline **6** generated



on reacting the oxime **4** with the olefin **5** in the presence of $NaOCl/Et_3N/H_2O/CH_2Cl_2$. The synthesis scheme is sufficiently flexible and efficient so as to be of practical use in the preparation of suitable quantities of this material for biological evaluation.

We disclose herein a total synthesis approach to the toxic metabolite, talaromycin B, product of the toxicogenic fungus *Talromyces stipitatus* isolated from a wood-shavings-based chicken litter.[1] The present literature indicates that the toxicity of this substance may be due to its ability to block outward potassium fluxes, thus leading to muscle dysfunction.[2] Talaromycin B represents but one of now many spiroketal structures to be produced by nature. It is the first, however, to be recognized as being elaborated by a fungus.[1] Others, which vary in structure from stereochemically complex to simple, have bacterial[3] or insect origins.[4]

(1) Lynn, D. G.; Phillips, N. J.; Hutton, W. C.; Shabanowitz, J.; Fennell, D. I.; Cole, R. J. *J. Am. Chem. Soc.* **1982**, *104*, 7319.
(2) See footnote 18 of ref 1.
(3) Westley, J. W. *Adv. Appl. Microbiol.* **1977**, *22*, 177. Westley, J. W. "The Polyether Antibiotics: Carboxylic Acid Ionophores"; Westley, J. W., Ed.; Marcel Dekker: New York, 1982; Chapter 1. Wierenga, W. "The Total Synthesis of Natural Products"; ApSimon, J., Ed.; Wiley: New York, 1981; Vol. 4, pp 263–351.
(4) Baker, R.; Herbert, R. H.; Parton, A. H. *J. Chem. Soc., Chem. Commun.* **1982**, 601 and references cited therein.

0002-7863/84/1506-0353$01.50/0