

**B. With Phosphorus Oxychloride and Pyridine.**—To a solution of 3.0 ml (5.02 g or 33 mmoles) of phosphorus oxychloride in 50 ml of anhydrous pyridine was added 8.287 g (41.4 mmoles) of the hydroxy ketal 4. After the reaction mixture had been heated on a steam bath for 1 hr, it was diluted with 10 ml of water and extracted successively with ether and with chloroform. The combined organic extracts were washed with dilute, aqueous hydrochloric acid and with aqueous sodium bicarbonate. After the organic phase had been dried and concentrated, the residual yellow liquid (10.44 g containing<sup>14</sup> three components believed to be ketones 1 and 6 and the ethylene ketal of ketone 1) was diluted with 100 ml of chloroform and stirred at room temperature with 50 ml of aqueous 6 M hydrochloric acid for 24 hr. The chloroform layer was separated, combined with the chloroform extract of the aqueous phase, washed with aqueous sodium bicarbonate, dried, concentrated, and distilled to separate 4.699 g of pale yellow liquid, bp 83–100° (14 mm), which contained<sup>14</sup> the unconjugated ketone 1 (64%, eluted first), the conjugated ketone (31%, eluted third), and a minor, unknown component (5%, eluted second) thought to be the ethylene ketal of ketone 1. The infrared and nmr spectra of this mixture are fully consistent with this composition. The product mixture from this reaction was combined with a comparable mixture from another reaction (total weight 11.25 g) and fractionally distilled to separate 2.83 g of the pure unconjugated ketone 1, bp 78–79° (18 mm),  $n_{D}^{25}$  1.4756–1.4767.

**cis-3-(2-Hydroxy-2-propyl)cyclohexanol.**—An ethereal solution containing 0.80 mole of methylmagnesium iodide was treated with 10.0 g (0.0794 mole) of the lactone of *cis*-3-hydroxycyclohexanecarboxylic acid.<sup>17</sup> After the reaction mixture had been stirred for 20 hr, it was hydrolyzed with an aqueous solution (pH ~8) of ammonia and ammonium chloride. The ethereal layer was combined with the ethereal extract of the aqueous phase and this organic solution was dried, concentrated, and distilled to separate 8.062 g of viscous liquid, bp 85–108° (0.05 mm), which crystallized on standing. Recrystallization from a carbon disulfide–ether mixture afforded 2.532 g of pure *cis*-3-(2-hydroxy-2-propyl)cyclohexanol as white prisms, mp 90.5–91°. The product has infrared absorption<sup>18</sup> at 3600 and 3440  $\text{cm}^{-1}$  (unassociated and associated OH) with broad nmr peaks<sup>19</sup> in the regions  $\delta$  3.3–4.0 (1 H, >CHO) and 0.9–2.8 (aliphatic CH) as well as a singlet at 1.22 (6 H,  $\text{CH}_3\text{C}$ ). The mass spectrum exhibits no molecular ion peak (the highest fragment peak is at  $m/e$  125) but has relatively abundant fragment peaks at  $m/e$  82, 67, 59, and 43.

*Anal.* Calcd for  $\text{C}_9\text{H}_{18}\text{O}_2$ : C, 68.31; H, 11.47. Found: C, 68.11; H, 11.35.

**Preparation of 3-Isopropenylcyclohexanone (1) from 2-Cyclohexen-1-one.**—Commercial 2-bromopropene<sup>20</sup> was washed successively with aqueous sodium sulfite and with aqueous sodium bicarbonate, then dried over calcium sulfate, and fractionally distilled to give the bromo olefin, bp 48.6–49.0.<sup>21</sup> The reaction of this bromide with magnesium was initiated by adding a few drops of the alkenyl halide to a mixture of 3.65 g (0.15 g-atom) of magnesium, 100 ml of tetrahydrofuran, and a crystal of iodine.<sup>22</sup> Then a total of 24.90 g (0.21 mole) of 2-bromopropene in 40 ml of tetrahydrofuran was added over a 1.5-hr period; the reaction mixture was then refluxed for 15 min at which time all the magnesium had been consumed. The solution was diluted with 100 ml of tetrahydrofuran (to prevent precipitation of the reagent at 0°) and cooled to 0°; then 1.4 g (0.0074 mole, 5 mole % based on the magnesium employed) of anhydrous cuprous iodide was added. Although a transient yellow color (*cf.* ref 2) was observed during this addition, the final cold solution was essentially black in color presumably because of the presence of colloidal metal particles. A solution of 6.80 g (0.071 mole) of 2-cyclohexen-1-one in 50 ml of tetrahydrofuran was added,

(17) The preparation of this lactone was described previously; see ref 10 and H. O. House, H. Babad, R. B. Toothill, and A. W. Noltes, *J. Org. Chem.*, **27**, 4141 (1962).

(18) Determined as a solution in chloroform.

(19) Determined as a solution in deuteriochloroform.

(20) Columbia Organic Chemicals Co., Inc., Columbia, S. C.

(21) (a) The commercial material contained<sup>15</sup> (in order of increasing retention times) an unidentified low-boiling component (2%), 2-bromopropene (60%), *cis*-1-bromopropene (26%), *trans*-1-bromopropene (11%), and 3-bromopropene (2%). The 2-bromopropene utilized in this experiment was approximately 96% pure.<sup>15</sup> (b) E. A. Braude and E. A. Evans [*J. Chem. Soc.*, 3333 (1956)] report bp 48°. (c) K. E. Harwell and L. F. Hatch [*J. Am. Chem. Soc.*, **77**, 1682 (1955)] report bp 47° (745 mm.).

(22) The general procedure of H. Normant, *Advan. Org. Chem.*, **2**, 1 (1960).

dropwise and with stirring over a 20-min period, to the cold (0°) organometallic solution, and the resulting mixture was stirred at 0° for 1 additional hr. The reaction mixture was then added to a cold (0°) aqueous solution (pH ~8) of ammonia and ammonium chloride and the organic layer was separated and combined with the ethereal extract of the aqueous phase. The combined organic solutions were dried, concentrated, and distilled in a short-path still. Fractional distillation of this product (which contained<sup>14</sup> the ketone 1 and low-boiling impurities) afforded 6.616 g (68%) of fractions, bp 80.5–84° (8 mm),  $n_{D}^{25}$  1.4743–1.4749, which contained<sup>14</sup> more than 97% of 3-isopropenylcyclohexanone (1). This product was identified with the previously described sample by comparison of infrared spectra and gas chromatographic retention times.

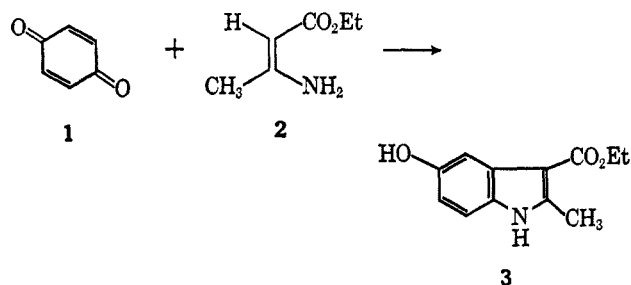
## The Nenitzescu Condensation of Ethyl 3-Aminocrotonate and 1,4-Benzoquinone<sup>1</sup>

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A general synthetic route to the 5-hydroxyindole nucleus, first described by Nenitzescu,<sup>2,3</sup> involves the condensation of a 1,4-benzoquinone with an appropriate 3-aminocrotonate as illustrated below for the preparation of 2-methyl-3-carbomethoxy-5-hydroxyindole (3). Our interest in the construction of various indole skeletons, in particular those bearing a free hydroxyl group at C-5,<sup>4</sup> led us to investigate this reaction.



Two products crystallized directly from the reaction of 1,4-benzoquinone (1) and excess ethyl 3-aminocrotonate (2) in refluxing dichloroethane. One component was identified as hydroquinone by comparison with authentic material. The other material, mp 200–201°, showed infrared absorptions anticipated for ethyl 2-methyl-3-carbomethoxy-5-hydroxyindole (3). This assignment was confirmed by an nmr spectrum which verified the presence of an ethyl ester, a singlet methyl group at C-2, and three aromatic protons whose split-

(1) Partial support of this work by the Petroleum Research Fund (196-G) and by the Michigan State All-University Fund is gratefully acknowledged.

(2) C. D. Nenitzescu, *Bull. Soc. Chim. Romania*, **11**, 37 (1929); *Chem. Abstr.*, **24**, 110<sup>s</sup> (1930).

(3) This reaction has subsequently been investigated by a number of workers: (a) R. J. S. Beer, K. Clark, H. F. Davenport, and A. Robertson, *J. Chem. Soc.*, 2029 (1951); (b) R. J. S. Beer, K. Clark, and A. Robertson, *ibid.*, 1262 (1953); (c) H.-J. Teuber and G. Thaler, *Chem. Ber.*, **91**, 2253 (1958); (d) E. A. Steck, R. P. Brundage, and L. T. Fletcher, *J. Org. Chem.*, **24**, 1750 (1959); (e) G. Domschke and J. Furst, *Chem. Ber.*, **92**, 3244 (1959); (f) A. N. Grinev, V. N. Ermakova, E. Vrotek, and A. P. Terent'ev, *Zh. Obshch. Khim.*, **29**, 2777 (1959); *Chem. Abstr.*, **54**, 10992e (1960), and preceding papers.

(4) Several naturally occurring 5-hydroxyindole bases show pronounced pharmacological activity: *cf.* R. H. F. Manske, "The Alkaloids," Vol. VIII, Academic Press Inc., New York, N. Y., 1965, pp 12–19.

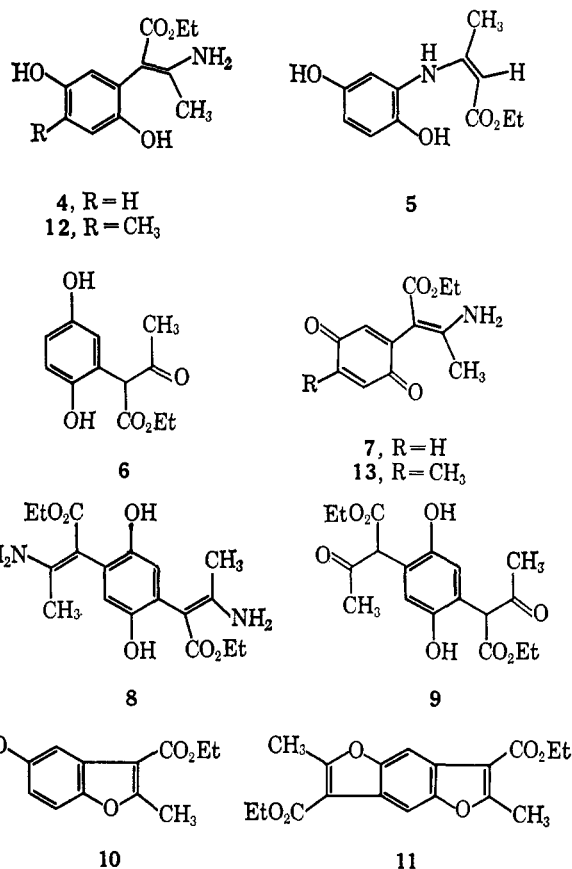
ting pattern was characteristic of 5-substituted indoles.<sup>5</sup> Further work-up of the reaction mixture furnished three additional products.

The major component of these, mp 140–143°, showed absorptions in the infrared attributable to unassociated NH, 3410 cm<sup>-1</sup> (sharp), and to hydrogen-bonded NH and/or OH, 3350 cm<sup>-1</sup> (broad). The carbonyl group absorption appeared as a doublet, 1650 and 1623 cm<sup>-1</sup>, which is characteristic of the 3-aminocrotonate chromophore.<sup>6</sup> An nmr spectrum revealed three aromatic protons as a one-proton doublet at  $\delta$  6.58 ( $J = 2$  cps) and as a two-proton multiplet at 6.73; signals at  $\delta$  1.17 (triplet,  $J = 7$  cps), 4.09 (quartet,  $J = 7$  cps), and 1.84 (singlet) were assigned to an ethyl ester and vinyl methyl groupings. These spectral data are consistent with a monosubstituted hydroquinone skeleton which contains a 3-aminocrotonate moiety. Two structures, **4** and **5**, satisfy these criteria and both are easily envisioned from the starting materials. They differ, however, in that structure **5** possess a vinyl proton, which appears at  $\delta$  4.45 in the nmr spectrum of **2**, while **4** contains no vinyl protons. Careful examination of the nmr spectrum of the aforementioned solid in the  $\delta$  4–5 region showed no absorption attributable to a vinyl proton. Consequently structure **4** can be assigned tentatively to the solid, mp 140–143°. Confirmation of this assignment was achieved by acid-catalyzed hydrolysis of **4** to the corresponding ethyl 2-(2,5-dihydroxyphenyl)acetoacetate (**6**) which was cyclized with zinc chloride to the known 2-methyl-3-carbethoxy-5-hydroxybenzofuran (**10**). This material was identical in all respects with a synthetic sample.<sup>9</sup>

The second product, mp 216–219°, showed absorptions in the infrared similar to those of **4** but its insoluble nature precluded an nmr analysis. This material was subjected to the hydrolysis and cyclization sequence described above. The resulting crystalline product showed *no* absorption in the infrared above 3100 cm<sup>-1</sup> and was identified as 2,6-dimethyl-3,7-dicarbethoxybenzo[1,2-*b*:4,5-*b'*]difuran (**11**) by direct comparison with an authentic sample.<sup>10</sup> Thus structure **8** can be assigned to the solid, mp 216–219°, while structure **9** corresponds to its hydrolysis product.

Preliminary spectral evidence suggested that the third product, a brilliant yellow material, mp 174–176, was simply the quinone **7** corresponding to **4** and it was not investigated further.

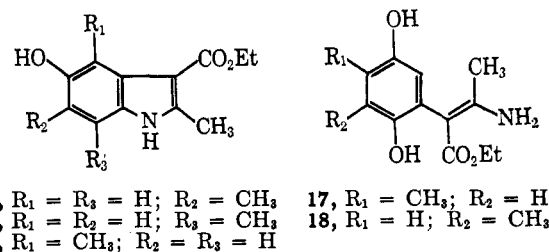
At the outset of this investigation two general mechanisms<sup>8b,c</sup> for the Nenitzescu condensation had been advanced. One of these<sup>8b</sup> proposed the intermediacy of the hydroquinone **4** which subsequently cyclized to the 5-hydroxyindole **3** in an unspecified manner. In our hands the thermal conversion of **4** to **3** was unsuccessful. Quite recently, however, Allen and Weiss<sup>8</sup> have shown that the hydroquinone **12** is an intermediate in the Nenitzescu condensation of toluquinone and **2**. These



workers have elegantly demonstrated that an oxidation-reduction pathway *via* quinone **13** is operative in the conversion of **12** to 2,6-dimethyl-3-carbethoxy-5-hydroxyindole (**14**). It seems probable that a similar mechanism is followed in the present reaction. The isolation of **8** suggests that the intermediate quinone **7** can also undergo further condensation with ethyl 3-aminocrotonate (**2**).<sup>12</sup>

In a typical experiment the following yields of isolated material (based on starting benzoquinone) were obtained: hydroquinone, 25%; 5-hydroxyindole **3**, 30%; monosubstituted hydroquinone **5**, 15%; quinone **7** and disubstituted hydroquinone **9**, approximately 10%. If it is assumed that some or all of the hydroquinone originates from nonindole productive pathways, these data account for 80–95% of the starting benzoquinone.

The condensation of toluquinone with **2** furnished the isomeric 2,6- and 2,7-dimethyl-3-carbethoxy-5-hydroxyindoles (**14** and **15**) and the hydroquinone **17** in agreement with Allen and Weiss.<sup>8,13</sup> In addition, a fourth, amorphous material was assigned structure **18**



**14**, R<sub>1</sub> = R<sub>3</sub> = H; R<sub>2</sub> = CH<sub>3</sub>    **17**, R<sub>1</sub> = CH<sub>3</sub>; R<sub>2</sub> = H  
**15**, R<sub>1</sub> = R<sub>2</sub> = H; R<sub>3</sub> = CH<sub>3</sub>    **18**, R<sub>1</sub> = H; R<sub>2</sub> = CH<sub>3</sub>  
**16**, R<sub>1</sub> = CH<sub>3</sub>; R<sub>2</sub> = R<sub>3</sub> = H

(5) G. Van Binst, C. Danheux, C. Hootel, J. Pecher, and R. H. Martin, *Tetrahedron Letters*, 973 (1964).

(6) K. Nakanishi, "Infrared Absorption Spectroscopy—Practical," Holden-Day, Inc., San Francisco, Calif., 1962, p 43.

(7) The *trans* configuration (amine-ring) accords with the nmr data (see Experimental Section and ref 8).

(8) G. R. Allen, Jr., and M. J. Weiss, *Chem. Ind. (London)*, 117 (1966).

(9) E. Bernatek and T. Ledaal, *Acta Chem. Scand.*, **12**, 2053 (1958).

(10) A. N. Grinev and A. P. Terent'ev, *Vestn. Mosk. Univ., Ser. Mat., Mekhan., Astron., Fiz. i Khim.*, **12**, No. 6, 147 (1957); *Chem. Abstr.*, **63**, 3187a (1959).

(11) The *trans* configuration (amine-ring) has been arbitrarily depicted.

(12) Also see D. Raileanu and C. D. Nenitzescu, *Rev. Roumaine Chim.*, **10**, 339 (1965); *Chem. Abstr.*, **63**, 9903 (1965).

(13) G. R. Allen, Jr., C. Pidacks, and M. J. Weiss, *Chem. Ind. (London)*, 2096 (1965).

from spectral data (see Experimental Section for details). No material corresponding to the isomeric 4-methylindole **16** was observed.

It is interesting to note in the various nmr spectra that the carbethoxy group at the 3 position exerts a considerable paramagnetic shielding effect on both the C-4 hydrogen atom and the C-2 methyl group. A similar effect was observed for 3-acetylindole and the benzofurans **10** and **11** (see Experimental Section).

### Experimental Section

Melting points were observed on a Kofler micro hot stage and are corrected. Infrared spectra were recorded on a Perkin-Elmer Model 237 grating infrared spectrometer. Nmr spectra were measured on a Varian Associates Model A-60 instrument and the chemical shifts are reported in parts per million ( $\delta$  values) downfield from tetramethylsilane. Thin layer chromatography (tlc) on silica gel G was routinely employed. Plates were developed with benzene-methanol (85:15 v/v) and were visualized with iodine vapors or ultraviolet light. Microanalysis were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

**Nenitzescu Condensation with 1,4-Benzoquinone.**—In a typical experiment, a solution of freshly sublimed 1,4-benzoquinone (**1**) (1.73 g, 16 mmoles) in 9 ml of 1,2-dichloroethane was added over a 20-min period to a stirred, refluxing solution of ethyl 3-aminocrotonate<sup>14</sup> (**2**) (3.00 g, 23 mmoles) in 10 ml of 1,2-dichloroethane under a nitrogen atmosphere. This mixture was heated under reflux for an additional 30 min, cooled, and filtered to yield a straw-colored solid. Tlc analysis of this material revealed two components.

**2-Methyl-3-carbethoxy-5-hydroxyindole (3).**—The straw-colored solid from above was washed with hot diethyl ether and the residue was crystallized from acetone-water to yield 1.06 g (30%) of product: mp 200–201° (lit. 205, 210<sup>3d</sup>);  $\nu_{\max}^{\text{Nujol}}$  3360, 3250, 1655, and 1625  $\text{cm}^{-1}$ ; nmr (methanol) 1.50 (3 H, triplet,  $J = 8$  cps), 2.72 (3 H, singlet), 6.70 and 6.84 (1 H, two doublets,  $J = 2$  and 9 cps), 7.21 (1 H, doublet,  $J = 9$  cps), and 7.38 (1 H, doublet,  $J = 2$  cps).

**Isolation of Hydroquinone.**—The combined mother liquors and ether washes from the purification of **3** were evaporated *in vacuo* to give a brownish residue, 460 mg (25%), which was mainly hydroquinone (nmr and tlc). Recrystallization from ether-hexane furnished white plates, mp 167–169°, mmp (with authentic hydroquinone) 169–171°. The infrared spectrum was identical with that of authentic material.

**Ethyl 3-Amino-2-(2,5-dihydroxyphenyl)crotonate (4).**—The dichloroethane mother liquors from the original reaction mixture slowly deposited 620 mg (16%) of a tan solid when allowed to stand at 0°. This material was collected, washed with hot diethyl ether, dissolved in acetone, and filtered free of insoluble residue. The clear acetone solution was evaporated *in vacuo* and the resulting solid was crystallized from acetonitrile to furnish product: mp 140–143°;  $\nu_{\max}^{\text{Nujol}}$  3410 (sharp), 3350 (broad), 1650, and 1623  $\text{cm}^{-1}$ ; nmr (acetone)  $\delta$  1.17 (3 H, triplet,  $J = 7$  cps), 1.84 (3 H, singlet), 4.09 (2 H, quartet,  $J = 7$  cps), 6.58 (1 H, doublet,  $J = 2$  cps), and 6.73 (2 H, multiplet).

Trace amounts of **8** (tlc) were still present after repeated crystallizations of **4**.

*Anal.* Calcd for  $\text{C}_{12}\text{H}_{15}\text{NO}_4$ : C, 60.75; H, 6.37; N, 5.90. Found: C, 60.27; H, 6.45; N, 6.71.

**2,5-Disubstituted Hydroquinone 8.**—After prolonged standing at 0° (45 days) the dichloroethane mother liquors furnished a second, extremely insoluble material. This solid was washed several times with hot acetonitrile to yield a white powder (homogeneous by tlc). This was then dissolved in a large excess of boiling dioxane, filtered free of insoluble residue, and evaporated *in vacuo* to give a yellow-white solid. Repeated trituration with boiling acetonitrile furnished a white crystalline powder: mp 216–219°;  $\nu_{\max}^{\text{Nujol}}$  3430, 3375, 3310, 1645, and 1620  $\text{cm}^{-1}$ .

*Anal.* Calcd for  $\text{C}_{15}\text{H}_{24}\text{N}_2\text{O}_6$ : C, 59.33; H, 6.64; N, 7.69. Found: C, 59.30; H, 6.67; N, 7.78.

**Quinone 7.**—This brilliant yellow material was obtained in varying amounts directly from the dichloroethane mother liquors and from the ether-soluble fractions obtained during normal

work-up. It was invariably contaminated with one or more of the other reaction products and was purified by tedious fractional crystallization from acetonitrile to yield yellow needles, mp 174–176°,  $\nu_{\max}^{\text{Nujol}}$  1685  $\text{cm}^{-1}$ .

**Hydrolysis of 4.**—A solution of 84 mg of **4** in 3 ml of acetone-water (1:1) containing 1 drop of acetic acid was heated under reflux in a nitrogen atmosphere for 2.5 hr to give a clear, pale yellow solution. This solution was diluted with water and extracted with methylene chloride. The organic phase was dried (sodium sulfate) and evaporated *in vacuo* to yield 81 mg of a yellow oil (**6**):  $\nu_{\max}^{\text{CHCl}_3}$  3600, 3400 (broad), 1725 (broad), 1640 (shoulder); nmr (methylene chloride)  $\delta$  1.22 (3 H, triplet,  $J = 7$  cps), 1.77 (singlet, enol methyl group), and 2.12 (singlet, keto methyl group, total 3 H, ratio of ca. 1:10, respectively), 6.76 (3 H, multiplet).

The aqueous phase was made alkaline with sodium hydroxide and ammonia was detected with moist pHYdron paper.

**Cyclization of 6 to 2-Methyl-3-carbethoxy-5-hydroxybenzofuran (10).**—A mixture of **6** (81 mg) and anhydrous zinc chloride (250 mg) in 3 ml of acetone containing 2 drops of acetic acid was heated under reflux for a total of 10 hr. The final yellow solution was diluted with water and extracted with methylene chloride. The organic phase was dried (sodium sulfate) and evaporated *in vacuo* to give a yellow solid. Crystallization from ethanol and acetonitrile yielded 20 mg of pure product, mp 134–137°, mmp (with authentic<sup>9</sup> **10**) 134–137°. The infrared spectrum was superimposable with that of authentic **10**. Tlc analysis of the mother liquors only showed the presence of **10** and unreacted starting material **6**.

**Hydrolysis of the 2,5-Disubstituted Hydroquinone 8.**—A 106-mg sample of **8** was hydrolyzed as described for **4** to yield 95 mg of a yellow oil (**9**):  $\nu_{\max}^{\text{CHCl}_3}$  3600, 3400 (broad), 1720 (broad), 1630, and 1605  $\text{cm}^{-1}$ ; nmr (methylene chloride)  $\delta$  1.24 (6 H, triplet,  $J = 7$  cps), 1.77 (singlet, enol methyl group), and 2.10 (singlet, keto methyl group, total 6 H, ratio of ca. 2:1, respectively), 6.50 and 6.75 (broad singlets, 2 H total, ratio of ca. 2:1, respectively).

Ammonia was detected in the aqueous phase as described above.

**Cyclization of 9 to 2,6-Dimethyl-3,7-dicarbethoxybenzo[1,2-b:4,5-b']difuran (11).**—A mixture of **9** (95 mg) and anhydrous zinc chloride (540 mg) in 5 ml of acetone containing 1 drop of acetic acid was heated under reflux for 2 hr. When cooled a white crystalline precipitate was deposited, 44 mg, mp 179–180°, mmp (with authentic<sup>10</sup> **11**) 179–182°. The infrared spectrum was identical with that of authentic **11**.

**2-Methyl-3-carbethoxy-5-hydroxybenzofuran (10)** was prepared by the method of Bernatek and Ledaa<sup>9</sup> in 50% yield. Repeated recrystallization from acetonitrile furnished pure product: mp 135–137° (lit.<sup>9</sup> mp 138°);  $\nu_{\max}^{\text{CHCl}_3}$  3600, 3350 (broad), 1700, 1625 (weak), and 1595  $\text{cm}^{-1}$ ; nmr (methanol)  $\delta$  1.48 (3 H, triplet,  $J = 7$  cps), 2.70 (3 H, singlet), 6.81 and 6.98 (1 H, two doublets,  $J = 3$  and 9 cps), 7.30 (1 H, doublet,  $J = 9$  cps) and 7.49 (1 H, doublet,  $J = 3$  cps).

**2,6-Dimethyl-3,7-dicarbethoxybenzo[1,2-b:4,5-b']difuran (11)** was obtained in 30% yield directly from the reaction described by Terent'ev, *et al.*,<sup>15</sup> as an ethanol-insoluble precipitate: mp 181–183° (lit.<sup>10</sup> mp 184°);  $\nu_{\max}^{\text{CHCl}_3}$  1700 and 1600  $\text{cm}^{-1}$ ; nmr (CDCl<sub>3</sub>)  $\delta$  1.45 (6 H, triplet,  $J = 7$  cps), 2.74 (6 H, singlet), and 7.81 (2 H, singlet). Tlc analysis of the ethanol-soluble material revealed hydroquinone and the benzofuran **10** as the major components.

**Nenitzescu Condensation with Toluquinone.**—The condensation of freshly sublimed toluquinone (2.04 g, 17 mmoles) and ethyl 3-aminocrotonate<sup>14</sup> (**2**) (3.00 g, 23 mmoles) was carried out as described above for 1,4-benzoquinone. After cooling, the reaction mixture was filtered to give a reddish solid and a dark red-brown filtrate (D). The crude solid was crystallized from acetone-water to furnish a white crystalline material (A); a second crop of straw-colored crystals (B) was obtained on partial evaporation and the dark red mother liquors were evaporated to dryness *in vacuo* to give a red gum (C).

**2,6-Dimethyl-3-carbethoxy-5-hydroxyindole (14).**—Tlc analysis of the white solid A revealed the presence of three components. Trituration with hot diethyl ether preferentially removed two of these. Crystallization of the remaining solid from ethanol furnished 347 mg of pure product: mp 225–226° (lit.<sup>13</sup> mp 228–229°);  $\nu_{\max}^{\text{Nujol}}$  3300 and 1660  $\text{cm}^{-1}$ ; nmr (methanol)  $\delta$

(14) Purchased from the Aldrich Chemical Co.

(15) A. N. Grinev, B.-K. Pan, and A. P. Terent'ev, *Zh. Obshch. Khim.*, **27**, 1087 (1957); *Chem. Abstr.*, **52**, 3761e (1958).

1.50 (3 H, triplet,  $J = 7$  cps), 2.35 (3 H, singlet), 2.70 (3 H, singlet), 7.10 (1 H, broad singlet), and 7.49 (1 H, singlet).

**2,7-Dimethyl-3-carboxy-5-hydroxyindole (15).**—Repeated recrystallization of the straw-colored solid B from ethanol gave 232 mg of pure product: mp 201–202° (lit.<sup>13</sup> mp 200–202°);  $\nu_{\text{max}}^{\text{Nujol}}$  3400, 3200 (broad), 1650, and 1600  $\text{cm}^{-1}$ ; nmr (methanol)  $\delta$  1.50 (3 H, triplet,  $J = 7$  cps), 2.48 (3 H, broad singlet), 2.73 (3 H, singlet), 6.56 (1 H, broad multiplet), and 7.35 (1 H, doublet,  $J = 3$  cps).

**Ethyl 3-Amino-2-(2,5-dihydroxy-4-methylphenyl)crotonate (17).**—Repeated trituration of the red gum C with diethyl ether gave a tan solid. Several crystallizations from acetone-methanol furnished 223 mg of pure product: mp 192–195° (lit.<sup>8</sup> mp 186–188°);  $\nu_{\text{max}}^{\text{Nujol}}$  3475, 3350 (broad), 1635, and 1590  $\text{cm}^{-1}$ ; nmr (methanol)  $\delta$  1.22 (3 H, triplet,  $J = 8$  cps), 1.83 (3 H, singlet), 2.25 (3 H, singlet), 6.51 (1 H, singlet), and 6.67 (1 H, slightly broadened singlet).

*Anal.* Calcd for  $\text{C}_{13}\text{H}_{17}\text{NO}_4$ : C, 62.14; H, 6.82; N, 5.57. Found: C, 62.24; H, 6.79; N, 5.51.

Tlc analysis of the combined residue, 900 mg, from the three purifications above revealed equal amounts of 14, 15, and 17. No further separation was undertaken.

**Ethyl 3-Amino-2-(2,5-dihydroxy-3-methylphenyl)crotonate (18).**—Repeated diethyl ether trituration of the red oil obtained by evaporation of the initial dichloroethane mother liquors (D) of the reaction furnished 45 mg of an amorphous solid which was homogeneous by tlc:  $\nu_{\text{max}}^{\text{Nujol}}$  3460, 3350, 1650, and 1615  $\text{cm}^{-1}$ ; nmr (methanol)  $\delta$  1.20 (3 H, triplet,  $J = 8$  cps), 1.80 (3 H, singlet), 2.23 (3 H, singlet), 6.38 (1 H, doublet,  $J = 3$  cps), and 6.61 (1 H, doublet,  $J = 3$  cps).

**Attempted Cyclization of 4 to 3.**—Repeated crystallization of 4 from acetonitrile or acetone resulted in some decomposition (red-brown mother liquors) but no apparent formation of 3 (tlc). A sample of 4 was heated under reflux in dichloroethane for 4 hr. and worked up in the normal manner. Thin layer chromatography revealed two transformation products, one with the same  $R_f$  value as 10, in addition to starting material 4; no 3 appeared to be formed.

**Nmr Spectra.**—Ethyl 3-aminocrotonate (2) showed (neat)  $\delta$  1.18 (3 H, triplet,  $J = 7$  cps), 1.87 (3 H, singlet), 4.07 (2 H, quartet,  $J = 7$  cps), and 4.45 (1 H, singlet).

**3-Acetylindole<sup>16</sup>** showed (methanol)  $\delta$  2.57 (3 H, singlet), 7.35 (3–4 H, broad multiplet), 8.14 (1 H, singlet), and 8.33 (1 H, multiplet).

Indole showed  $\delta$  6.80 (C-2 H).<sup>17</sup>

**6-Methoxytetrahydrocarbazole** showed  $\delta$  6.91 (C-4 H).<sup>5</sup>

**2-Methylindole** showed  $\delta$  2.20 (C-2  $\text{CH}_3$ ).<sup>17</sup>

(16) J. E. Saxton, *J. Chem. Soc.*, 3592 (1952).

(17) L. A. Cohen, J. W. Daly, H. Kny, and B. Witkop, *J. Am. Chem. Soc.*, **82**, 2184 (1960).

## The Question of Sulfoquinone Intermediates

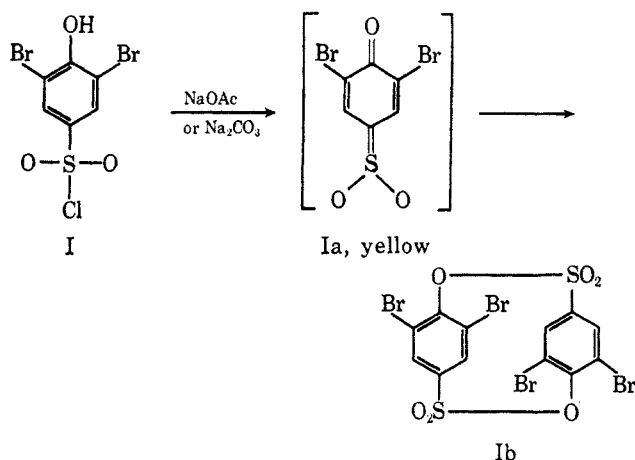
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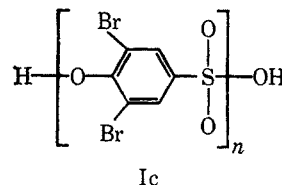
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Zincke and Brune<sup>1</sup> reported in 1908 that treatment of 3,5-dibromo-4-hydroxybenzenesulfonyl chloride (I) with either sodium acetate or carbonate in aqueous acetone resulted in the formation of a yellow solution; they attributed the color to the presence of an intermediate "quinoid sulfene" or sulfoquinone (Ia). The color was said to have faded during the reaction and a colorless precipitate thought to have structure Ib was formed.

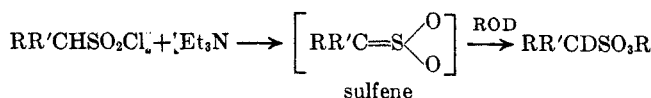
(1) (a) T. Zincke and R. Brune, *Ber.*, **41**, 902 (1908); (b) T. Zincke and W. Glahn, *ibid.*, **40**, 3039 (1907).



Oae and Kiritani<sup>2</sup> have recently re-examined this reaction and were unable to give further evidence for the intermediacy of the colored species Ia, but showed that the yellow solution had a clear maximum at 310  $\mu$ . They also examined the colorless product of this reaction and suggested that it was the linear oligomer Ic.



Evidence for the intermediacy of sulfenes has been reported recently in the reaction of sulfonyl chlorides with deuterated alcohols in the presence of triethylamine. The formation of monodeuterated sulfonate esters was rationalized by King and Durst<sup>3</sup> and Truce, *et al.*,<sup>4</sup> in terms of the following reaction scheme.



The latter findings prompted us to reinvestigate the work of Zincke and Brune<sup>1</sup> with the intention of trapping the sulfoquinone, Ia, and establishing its intermediacy in the reaction of phenolic sulfonyl chlorides with bases. For the purpose of doing this sulfonyl halides and esters were prepared and characterized (Table I).

TABLE I  
SULFONYL HALIDES AND ESTERS

Substituent	I	II	III	IV	V	VI
X	Br	Cl	$\text{CH}_3$	Cl	$\text{CH}_3$	$\text{CH}_3$
Y	Cl	Cl	Cl	F	F	$\text{OCH}_3$

(2) S. Oae and R. Kiritani, *Bull. Chem. Soc. Japan*, **38**, 1543 (1965).

(3) J. F. King and T. Durst, *J. Am. Chem. Soc.*, **86**, 287 (1964).

(4) W. E. Truce, R. W. Campbell, and J. R. Morell, *ibid.*, **86**, 288 (1964).