Reaction of 4-*tert*-Butylcatechol and Its Derivatives with Methoxy(pyridine)copper(II) Chloride in the Absence of Oxygen. A New Structure Reminiscent of Those Resulting from "Extradiol" Oxidations of Catechols in the Presence of Oxygen

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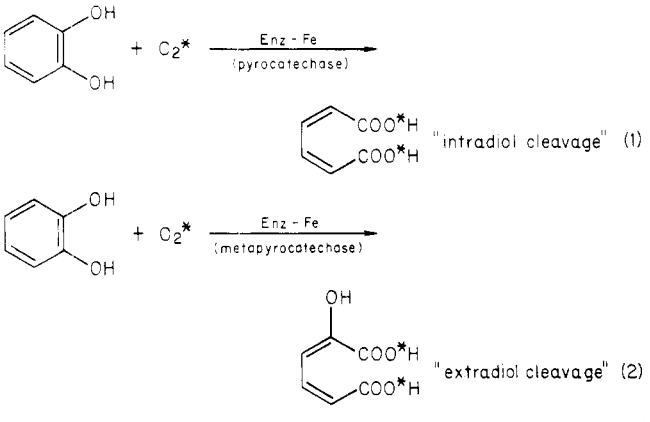
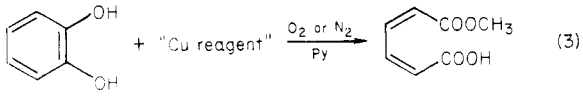
Reaction of methoxy(pyridine)copper(II) chloride with 4-*tert*-butylcatechol, 4-*tert*-butyl-1,2-benzoquinone, 4-*tert*-butyl-3-methoxycatechol, 4-*tert*-butyl-3-chlorocatechol, or 3,5-di-*tert*-butylcatechol in pyridine in the absence of oxygen provides 2,2-dimethoxy-6-(carbomethoxy)-4-*tert*-butyloxacyclohexa-3,5-diene as a major product. This novel six-electron oxidation of catechols is reminiscent of a well-known "extradiol" oxidation of catechol by metapyrocatechase, which, however, occurs only in the presence of molecular oxygen.

The copper-containing enzyme tyrosinase catalyzes selective oxidation of phenols and catechols to *o*-benzoquinones, and the iron-containing enzymes pyrocatechase and metapyrocatechase are known to catalyze oxidation of catechols to muconic acids or to hydroxylated muconic acid aldehydes.[1,2] Since labeling experiments showed that both oxygen atoms are incorporated in the reaction products of the catechol cleavage (eq 1 and 2), it is generally assumed that these enzyme molecules are capable of "activation of molecular oxygen".[1a]



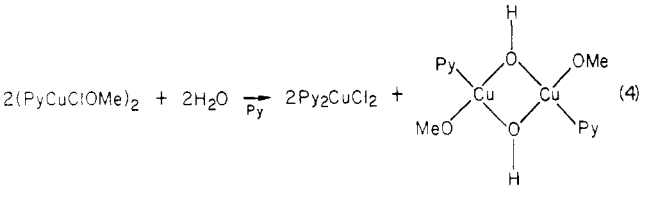
Recently we had demonstrated that analogous "intradiol cleavage" of catechols and *o*-benzoquinones can be carried out with certain copper(II) reagents under aerobic as well as *anaerobic* conditions[3-5] with equal facility (eq 3). Interestingly, one of the copper(II) reagents, methoxy(pyridine)copper(II) chloride,[4-6] in pyridine under *anaerobic and anhydrous* conditions provided a reaction product reminiscent of "extradiol cleavage" of catechols,[2] and the discussion of this reaction is the topic of this report.



Results and Discussion

In an earlier account we described in detail the oxidative carbon–carbon bond cleavage of *o*-benzoquinones, catechols, and phenols induced by certain copper(II) reagents in the presence as well as in the absence of molecular oxygen.[3-5] The reaction involves electron transfer from the organic substrate to the copper(II) reagent, followed by further transfer of electrons from the reduced copper species to molecular oxygen, regenerating the copper(II) state. In the discussion of the nature of the copper(II) reagent, we suggested that the dimeric or oligomeric cupric methoxide hydroxide was the active component of the copper(II) reagent and that the accompanying cupric chloride provided the thermodynamic driving force for complete oxidation.[4,5]

One of several methods[4,5] for generation of the copper(II) reagent involved addition of 1 molar equiv of water to methoxy(pyridine)copper(II) chloride dimer dissolved in pyridine (eq 4).



We now have found that a substantially different redox behavior between aromatic substrates and methoxy(pyridine)copper(II) chloride in pyridine takes place under strictly *anhydrous and anaerobic* reaction conditions.

(1) (a) For a general discussion including a discussion of the activation of molecular oxygen, see O. Hayaishi, "Molecular Mechanisms of Oxygen Activation", O. Hayaishi, Ed., Academic Press, New York, 1974, Chapter 1, and references therein; (b) A. J. M. Schoot-Viterkamp and H. S. Mason, *Proc. Natl. Acad. Sci. U.S.A.*, **70**, 993 (1973); (c) R. L. Jolley, L. H. Evans, N. Makino, and H. S. Mason, *J. Biol. Chem.*, **249**, 335 (1974); (d) N. Makino, P. McKahill, H. S. Mason, and T. H. Mass, *ibid.*, **249**, 6062 (1974).

(2) (a) O. Hayaishi, *Proc. Plenary Sess. Int. Congr. Biochem., 6th*, 31 (1964); (b) O. Hayaishi, *Bacteriol. Rev.*, **30**, 720 (1966); (c) A. Nakazava, Y. Kajima, and H. Taniuchi, *Biochim. Biophys. Acta*, **147**, 189 (1967); (d) R. N. Patel, C. T. Hou, A. Felix, and M. O. Lillard, *J. Bacteriol.* **127**, 536 (1976); (e) M. Fujiwara, L. A. Golovleva, Y. Sakei, M. Nozaki, and O. Hayaishi, *J. Biol. Chem.*, **250**, 4848 (1975); (f) for a review of other dioxygenases, see S. Dagley, "Survey of Progress in Chemistry", A. F. Scott, Ed., Academic Press, New York, 1977, p 121.

(3) M. M. Rogić, T. R. Demmin, and W. B. Hammond, *J. Am. Chem. Soc.*, **98**, 7441 (1976).

(4) M. M. Rogić and T. R. Demmin, *J. Am. Chem. Soc.*, **100**, 5472 (1978).

(5) M. M. Rogić and T. R. Demmin, "Aspects of Mechanism and Organometallic Chemistry", J. H. Brewster, Ed., Plenum Press, New York, 1978, p 141.

(6) H. Finkbeiner, A. S. Hay, H. S. Blanchard, and G. F. Endres, *J. Org. Chem.*, **31**, 549 (1966).

(7) W. Brackman and E. Havinga, *Recl. Trav. Chim. Pays-Bas*, **74**, 937 1021, 1070, 1100, 1107 (1955).

(8) It is perhaps not a coincidence that the active metal centers in metalloenzymes are located in the internal, hydrophobic region of the protein.

(9) For a suggestion that the "intradiol cleavage" of catechols, catalyzed by typical dioxygenases, may also be a special case of ionic, metal-induced, two-electron oxidation, see ref 5.

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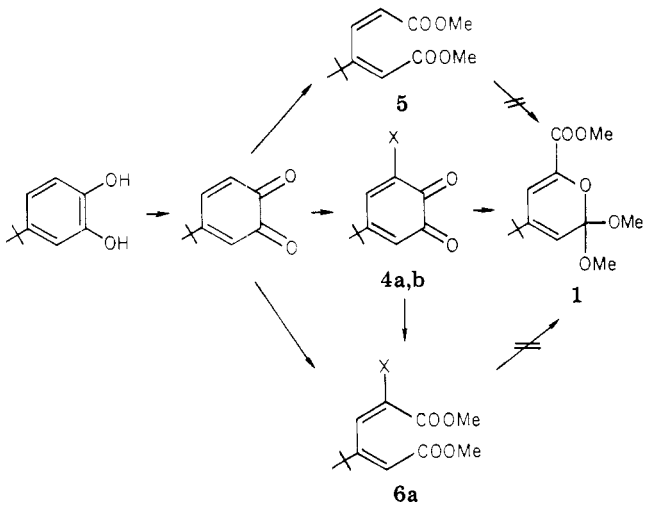
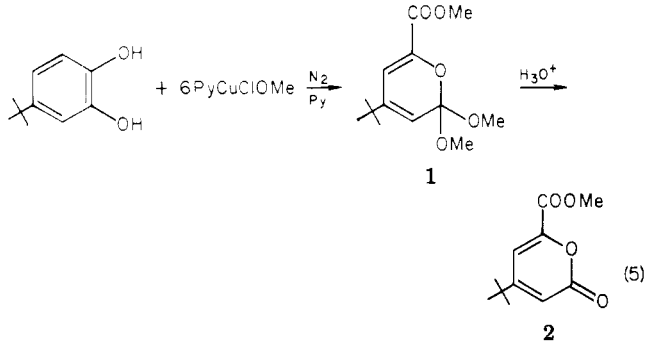
Scheme I

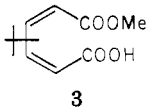


When phenol and methoxy(pyridine)copper(II) chloride are mixed in pyridine under nitrogen over an extended period of time, no net oxidation of phenol takes place. Under the same conditions, reaction of catechol with methoxy(pyridine)copper(II) chloride provides an undefined polymer mixture. However, under the same reaction conditions, 4-*tert*-butylcatechol reacts with an excess of methoxy(pyridine)copper(II) chloride to give 2,2-dimethoxy-6-(carbomethoxy)-4-*tert*-butyloxacyclohexa-3,5-diene (**1**) in 64% yield (eq 5). A simple evaporation of the



(5)

solvent after complete reaction and pentane extraction of the resulting solid residue, followed by the removal of pentane, afforded the ortho ester. If, on the other hand, the reaction mixture was hydrolyzed directly and then worked up or if the ortho ester was treated with the aqueous acid, the corresponding α-pyrone, 6-(carbomethoxy)-4-*tert*-butyloxacyclohexa-3,5-dien-2-one (**2**), was obtained. The monomethyl esters of *tert*-butylmuconic acid (**3**), produced in high yield under aerobic conditions or in

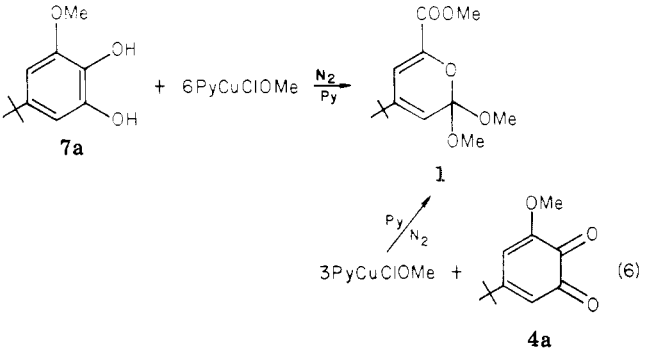


the anaerobic reaction with the copper(II) reagent [methoxy(pyridine)copper(II) chloride in pyridine in the presence of 1 molar equiv of water],[3-5] are observed only in very small amounts. The remainder of the crude product appears to be a mixture of several unidentified species.

4-*tert*-Butyl-1,2-benzoquinone under similar reaction conditions reacts with half as much of methoxy(pyridine)copper(II) chloride (relative to 4-*tert*-butylcatechol) and gives the ortho ester 1 in about the same yield.

Possible Reaction Pathways Leading to Ortho Esters. There are several possible reaction pathways outlined in Scheme I which may reasonably account for the observed six-electron oxidation of 4-*tert*-butylcatechol to ortho ester **1**. The most probable pathway could involve the *o*-benzoquinone **4** (**4a**, X = OMe; **4b**, X = Cl); however, other possibilities must also be considered.

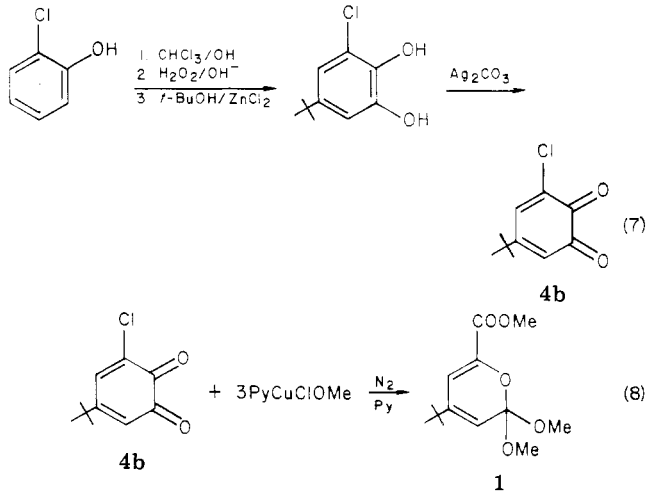
Thus, neither the dimethyl ester of 3-*tert*-butylmuconic acid (**5**) nor the further oxidized diester **6a** (X = OCH_3) reacted with an excess of methoxy(pyridine)copper(II) chloride in pyridine under anaerobic and anhydrous conditions. On the other hand, both 3-methoxy-5-*tert*-butylcatechol[10] (**7a**) and the *o*-benzoquinone[10] **4a** under the same conditions provided the ortho ester **1** in high yield (eq 6). Moreover, when the reaction was performed with



(6)

a 1:1 mixture of the diester **6a** and *o*-benzoquinone **4a**, only the **4a** was converted to the ortho ester **1**, the diester **6a** being recovered quantitatively. This clearly shows that there is not a reactive species formed from **4a** that is capable of converting **6a** to **1**, and, therefore, **6a** as well as **5** are excluded from further consideration regarding the possible mechanism.

The fact that **4a** affords the ortho ester **1** does not eliminate the possibility that in a direct oxidation of 4-*tert*-butylcatechol, 4-*tert*-butyl-1,2-benzoquinone, or 3-methoxy-5-*tert*-butylcatechol **7a** some additional or different intermediate other than **4a** may be involved. As mentioned above, 3-chloro-4-*tert*-butyl-1,2-benzoquinone appears as the only other reasonable intermediate that, if produced by a kinetic oxidation under the present reaction conditions, could provide the ortho ester **1** in a further two-electron oxidation. Indeed, the reaction of 3-chloro-5-*tert*-butyl-1,2-benzoquinone (**4b**) with methoxy(pyridine)copper(II) chloride in pyridine under anaerobic and anhydrous conditions gave the ortho ester **1** in comparable yield with that from the *o*-benzoquinone **4a** (eq 7 and 8). Consequently, the question as to whether



(7)

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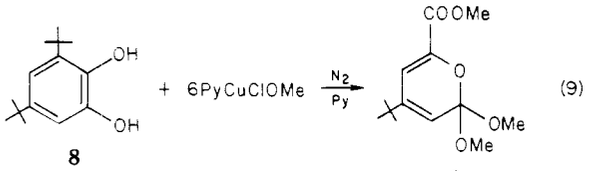
(10) T. R. Demmin and M. M. Rogić, *J. Org. Chem.*, **45**, 1153 (1980).

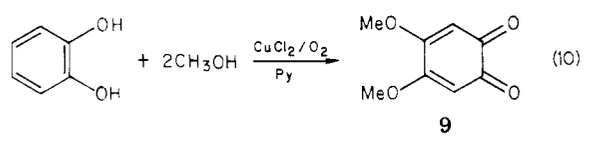
4-*tert*-butyl-1,2-benzoquinone undergoes a two-electron oxidation to give first the corresponding 3-chloro intermediate (which is then displaced by methoxide to give **4a**) remains open. Interestingly, even the reaction of 3,5-di-*tert*-butylcatechol (**8**) with methoxy(pyridine)copper(II) chloride in pyridine under anaerobic and anhydrous conditions gave the ortho ester **1** as a major product (eq 9).



8 1 (9)

Nature of the Active Copper(II) Species. The active component of the copper(II) reagent responsible for the four-electron oxidation of catechols to the monomethyl ester of muconic acid was shown to be dimeric or oligomeric cupric methoxide hydroxide.[4,5] In the present reaction this key copper(II) species cannot be generated by methoxy(pyridine)copper(II) chloride reacting with 4-*tert*-butylcatechol (or 4-*tert*-butyl-1,2-benzoquinone) by any reasonable route under anaerobic and anhydrous conditions in pyridine. Thus, ester formation is precluded, and a different pathway prevails, one leading to a net six-electron oxidation product, **1**.

While cupric methoxide chloride reacts with pyridine to give methoxy(pyridine)copper(II) chloride,[6] and both reagents in pyridine in the presence of 1 molar equiv of water gave the same copper(II) reagent as a 1:1:1 mixture of cupric methoxide, cupric chloride, and water,[4,5] a 1:1 mixture of cupric chloride and cupric methoxide in pyridine does not provide methoxy(pyridine)copper(II) chloride.[6] Consequently, it is not surprising that there was no reaction between 4-*tert*-butylcatechol and cupric chloride in pyridine in the absence of oxygen and water. The reaction with cupric methoxide, on the other hand, provides the corresponding monocopper catecholate–pyridine complex.[4] Earlier we showed that this copper catecholate was stable to an excess of cupric methoxide, but it underwent a reaction with cupric chloride, giving a polymeric material[4] which was not characterized. The same reaction also occurs when 4-*tert*-butylcatechol is allowed to react with a 1:1 mixture of cupric chloride and cupric methoxide. Brackman and Havinga demonstrated that copper-catalyzed oxidation of phenol and catechol, in the presence of nucleophiles, involves an oxidative Michael-type addition.[7] These oxidations proceed relatively slowly, presumably via a series of *one-electron* transformations induced by the *monomeric* copper(II) ion. For example, methanol reacts with catechol and 4-*tert*-butylcatechol under oxygen in the presence of cupric chloride to give the expected Michael products **9** and **10** (eq 10 and 11).



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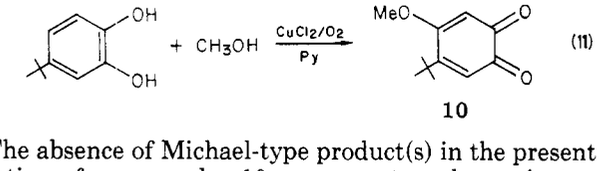

10 (11)

The absence of Michael-type product(s) in the present reaction, for example, **10**, argues strongly against a mechanism involving a one-electron transformation, a monomeric copper(II) species, and an external attack by methoxide. Thus, it appears that the ortho ester **1** is produced by an ionic two-electron process which, mechanistically, may be very similar to the proposed pathway for the copper(II)-induced cleavage of catechols and *o*-benzoquinones to the monomethyl ester of muconic acid.[4,5] However, unlike this transformation, the oxidative carbon–carbon bond cleavage in the present reaction is preceded by a two-electron oxidation that leads either to formation of 3-methoxy- or 3-chloro-4-*tert*-butyl-1,2-benzoquinone, which then undergoes the final two-electron oxidation to give the ortho ester **1**. The details of individual reaction steps and the nature of the intermediates involved are, however, not known at this time.

Conclusions

Unlike aerobic four-electron oxidative "extradiol cleavage" of catechols catalyzed by numerous dioxygenases,[1,2] the described cleavage of 4-*tert*-butylcatechol and related substrates, induced by methoxy(pyridine)copper(II) chloride in pyridine, occurs with great facility under anaerobic conditions. The reaction involves a prior two-electron oxidation of 4-*tert*-butylcatechol or *o*-benzoquinones at the more readily accessible ortho carbon to produce either a 3-methoxy- or a 3-chloro derivative which then undergoes the carbon–carbon bond cleavage reaction to give the ortho ester **1**. While the reaction product is reminiscent of the products observed in enzymatic "extradiol cleavage" reactions, the precise site of the carbon–carbon cleavage leading to this product is not yet known. A remarkable aspect of this reaction, besides the fact that it takes place in the absence of oxygen, is that it occurs under anhydrous conditions.[8] Evidently, small variations in reaction conditions have a large effect on the nature of the active copper species and on the reaction course itself.[3-5] This novel transformation is still another example of the reaction previously observed with dioxygenases only in the presence of oxygen, suggesting that even enzymatic "extradiol cleavage" may be a special case of a typical ionic, two-electron, metal-induced, oxidative carbon–carbon bond cleavage, with oxygen acting as the thermodynamic driving force by reoxiding the metal center to a higher oxidation state.[9]

Experimental Section

4-*tert*-Butylcatechol and 3,5-di-*tert*-butylcatechol were commercial products. Other derivatives were either prepared according to literature procedures or prepared as reported below. Methoxy(pyridine)copper(II) chloride was prepared as before.[4,6] Pyridine, used as a reaction solvent, was freshly distilled and degassed prior to use.

Boiling and melting points are uncorrected. GLC analyses were carried out on a Hewlett-Packard 5700A instrument using either 10% SE-30 on Chromosorb W or 10% Carbowax 20M with 3- or 6-ft columns. ^{1}H NMR spectra were recorded on Varian T60-A 60-MHz and HA-100 100-MHz instruments while ^{13}C NMR spectra were measured on a Varian CFT-20 instrument. All NMR spectra were measured by using tetramethylsilane as an internal standard. Routine chemical-ionization mass spectra were obtained on a Finnigan 3100D mass spectrometer.

General Procedure for Anaerobic, Anhydrous Oxidations with Methoxy(pyridine)copper(II) Chloride. Freshly dried pyridine (distilled from barium oxide) is placed in a dry three-neck flask equipped with a mechanical stirrer, a pump-driven syringe, and an inlet for the introduction of nitrogen or argon. The appropriate amount of methoxy(pyridine)copper(II) chloride is added, making an approximately 0.1 M solution, and the mixture freeze–pump–thaw degassed three times. The substrate in degassed pyridine is added at room temperature by the pump-driven syringe over 30–60 min, and then the mixture is stirred an additional 60 min. Evaporation at room temperature followed by extraction with pentane, or by hydrolysis, etc., provides the product.

2,2-Dimethoxy-6-(carbomethoxy)-4-*tert*-butyloxacyclohexa-3,5-diene (1). To a solution of methoxy(pyridine)copper(II) chloride (6.27 g, 30 mmol) in dry pyridine (60 mL) degassed as above was added a solution of 4-*tert*-butylcatechol (0.83 g, 5 mmol) and methanol (0.5 mL) in 10 mL of degassed pyridine via a pump-driven syringe at room temperature and under nitrogen with rapid stirring. After complete addition, the reaction mixture was stirred at room temperature for an additional 30 min, and then the solvent was evaporated in vacuo at room temperature. The resulting solid was extracted four times with pentane, and the pentane solution was dried over magnesium sulfate and evaporated to give the ortho ester 1 in 64% yield. The distillation provided a pure sample [bp 100 °C (0.06 mm)] as described previously.[4]

6-(Carbomethoxy)-4-*tert*-butyloxacyclohexa-3,5-dien-2-one (2). The same procedure was followed as above, but after the pyridine evaporation the residue was dissolved in degassed chloroform (250 mL) at 0 °C and hydrolyzed with 20% hydrochloric acid. Preparative TLC of the crude product afforded the α-pyrone ester **2** as a white solid, mp 84–85 °C.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with Methoxy(pyridine)copper(II) Chloride. By use of a procedure similar to that used above, 4-*tert*-butyl-1,2-benzoquinone was converted to the ortho ester **1** in a similar yield.

Dimethyl 2-Methoxy-4-*tert*-butyl-2,4-hexadienedioate (6a). The preparation of the methoxy diester by treating 3-methoxy-5-*tert*-butyl-1,2-benzoquinone (**4a**) with (1) *m*-chloroperoxybenzoic acid, (2) methoxy(pyridine)copper(II) chloride, and (3) diazomethane has already been described.[10]

Dimethyl 3-*tert*-Butylmuconate (5). A crude mixture of isomers of the monomethyl ester of β-*tert*-butylmuconic acid[4,5] (~8.7 g, ~41 mmol) was stirred with excess diazomethane in ether at 0 °C for 1 h and at room temperature overnight. Solvent removal gave 7.9 g of crude diester as an amber oil. Purification by evaporative distillation gave 3.40 g (37% yield) of diester **5** containing a mixture of double bond isomers (85:15 2*Z*,4*Z*/2*Z*,4*E*): bp 102 °C (0.7 mm); IR (thin film) 1730, 1655, 1628, 1442, 1200, 1170, 1020 cm^{-1}; UV (methanol) λ_{max} 207.5 nm (ϵ 153); mass spectrum (CI, methane), *m/e* 227 (MH^+); NMR ($CDCl_3$, 2*Z*,4*Z*) δ 6.72 (dd, *J* = 11.3, 1.9 Hz, CH=CHCO, 1), 5.95 (d, *J* = 11.3 Hz, CH=CHCO, 1), 5.80 (d, *J* = 1.9 Hz, =CHCO, 1), 3.62 (s, 2 CO_2CH_3, 6), 1.13 (s, $(CH_3)_3C$, 9); ^{13}C NMR ($CDCl_3$) δ 166.91 (CO), 165.83 (CO), 165.58 (=CC(CH_3)$_3$), 142.28 (CH=CHCO), 121.23 (CH=CHCO) 114.61 (=CHCO), 51.09 (CH_3O, two peaks superimposed?), 37.86 ($(CH_3)_3C$), 29.16 ($(CCH_3)_3C$).

Anal. ($C_{12}H_{18}O_4$) C, H.

Reaction of 3-Methoxy-5-*tert*-butylcatechol with Methoxy(pyridine)copper(II) Chloride. A degassed solution of methoxy(pyridine)copper(II) chloride (6.27 g, 30 mmol) and methanol (0.5 mL) in pyridine (60 mL) was treated with a degassed solution of 3-methoxy-5-*tert*-butylcatechol and methanol (0.3 mL) in pyridine (10 mL) according to the standard procedure. Evaporation and acid hydrolysis gave 1.10 g of amber oil shown by NMR to be >90% pure α-pyrone **2** (yield ca. 94%), with the remainder being unidentified material.

Reaction of 3-Methoxy-5-*tert*-butyl-1,2-benzoquinone[10] with Methoxy(pyridine)copper(II) Chloride. By use of a procedure similar to that described above, 3-methoxy-5-*tert*-butyl-1,2-benzoquinone was converted to α-pyrone **2** in ca. 90% yield. Prior to acid hydrolysis, a single pentane extraction afforded ortho ester ester 1 (ca. 20% yield) which was then combined with the remainder of the crude product for the acid hydrolysis step.

Reaction of 3-Methoxy-5-*tert*-butylcatechol/Dimethyl 2-Methoxy-4-*tert*-butyl-2,4-hexadiendioate Mixture with Methoxy(pyridine)copper(II) Chloride. By use of the standard anaerobic, anhydrous procedure, a mixture of 3-methoxy-5-*tert*-butylcatechol[10] (0.26 g, 1 mmol) and dimethyl 2-methoxy-4-*tert*-butyl-2,4-hexadiendioate (**6a**; 0.26 g, 1 mmol) was added to a solution of methoxy(pyridine)copper(II) chloride (2.50 g, 12 mmol) and methanol (0.12 mL) under nitrogen. Evaporation and thorough pentane extraction of the residue gave 0.47 g of clear, colorless oil, shown by NMR to be a mixture of ortho ester ester 1 and unreacted diester **6a** in a 57:43 ratio.

5-*tert*-Butyl-3-chloro-1,2-benzoquinone (4b). A solution of 2-chlorophenol (180 g, 1.40 mol) and benzyltriethylammonium chloride (3 g) in chloroform (1.4 L) was rapidly stirred at 0 °C in a 5-L Morton flask under nitrogen as 1.4 L of 50% aqueous sodium hydroxide was added over 1.5 h (**Caution**: exothermic). The reaction mixture was stirred an additional 2 h at 0 °C and then warmed cautiously to 50 °C (**Caution!**) and maintained at 50 °C for 5 h. Cooling to 0 °C followed by acidification to pH 1, layer separation, and steam distillation gave the crude product. Purification via the sodium bisulfite adduct provided 3-chloro-2-hydroxybenzaldehyde (53.5 g) in 25% yield.

5-*tert*-Butyl-3-chlorocatechol was prepared by using the *tert*-butylation procedure of Stockelbach.[11] Kugelrohr distillation of the crude product at 90–95 °C (0.3 mm) and recrystallization from pentane/chloroform afforded the pure catechol: mp 72–74 °C; mass spectrum (CI, methane), *m/e* 201 (MH^+ with one Cl present); NMR ($CDCl_3$) δ 6.90 (s, aromatic, 2), ~5.6 (br, OH, 2), 1.25 (s, $(CH_3)_3C$, 9).

5-*tert*-Butyl-3-chloro-1,2-benzoquinone (4b) was obtained by oxidation of a crude sample of 5-*tert*-butyl-3-chlorocatechol (~13 g, ~65 mmol) with excess silver carbonate on Celite in benzene (1 L). Upon filtration and evaporation the crude product was extracted with pentane and recrystallized from pentane at −30 °C to give ~4.30 g (33% yield) of 5-*tert*-butyl-3-chloro-1,2-benzoquinone (**4b**) as a red solid which, after sublimation at 50 °C (0.1 mm), had the following: mp 75–76 °C; IR (Nujol) 1708, 1673, 1625, 1560 cm^{-1}; UV (cyclohexane) λ_{max} 408 (ϵ 1360), 390 (1330, ~2600); mass spectrum (CI, methane), *m/e* 199 (MH^+ with one Cl present); NMR ($CDCl_3$) δ 7.25 (d, *J* = 2.1 Hz, CH=CCO, 1), 6.22 (d, *J* = 2.1 Hz, CHCO, 1), 1.23 (s, $(CH_3)_3$ C, 9); ^{13}C NMR ($CDCl_3$) δ 179.00 (C=O), 173.37 (C=O), 162.25 ($(CH_3)_3CC$=), 136.75 (CH=CCl), 132.29 (=CCl), 36.07 ($(CH_3)_3C$), 27.86 (CH_3).

Anal. ($C_{10}H_{11}ClO_2$) C, H.

Reaction of 5-*tert*-Butyl-3-chloro-*o*-benzoquinone (4b) with Methoxy(pyridine)copper(II) Chloride. The chloroquinone **4b** (0.4 g, 2 mmol) was oxidized with methoxy(pyridine)copper(II) chloride (1.25 g, 6 mmol) in dry pyridine (20 mL) under nitrogen according to the standard procedure. Evaporation and one pentane extraction (75 mL) gave ~0.1 g of colorless oil which was shown by NMR to be pure ortho ester ester **1**. Acid hydrolysis of this product cleanly produced α-pyrone **2**.

Oxidation of 4-*tert*-Butylcatechol with Cupric Chloride/Methanol in Pyridine Under Oxygen. Bis(pyridine)copper(II) chloride (2.09 g, 7.14 mmol) was added to a solution of methanol (0.5 mL) and dry pyridine (20 mL) with mechanical stirring at room temperature under an oxygen atmosphere. A solution of 4-*tert*-butylcatechol (0.83 g, 5 mmol) and methanol (0.5 mL) in pyridine (10 mL) was added over 60 min by a pump-driven syringe. After the mixture was stirred 20 h, 109 mL (4.9 mmol) of oxygen was consumed, and the reaction mixture was evaporated and acid hydrolyzed in the standard manner. By NMR analysis the viscous red-brown residue (0.82 g) contained ca. 75% 5-*tert*-butyl-4-methoxy-1,2-benzoquinone (**10**) plus traces of both isomers of the monomethyl ester of β-*tert*-butylmuconic acid (**3**) reported previously.[4]

5-*tert*-Butyl-4-methoxy-1,2-benzoquinone (10). Into a freshly prepared solution of sodium methoxide (61 mmol) in dry methanol (70 mL) was added lead dioxide (26.3 g, 110 mmol) under a nitrogen atmosphere with magnetic stirring at 15 °C. Then 4-*tert*-butylcatechol (4.15 g, 25 mmol) in methanol (20 mL) was added over 30 min via a pump-driven syringe to the rapidly stirred mixture maintained at 15–20 °C. After being stirred an additional 15 min, the mixture was quenched at 0 °C by the addition of 50% aqueous acetic acid (60 mL) over a period of 10 min, followed by extraction with chloroform (250 mL). The chloroform layer was washed with water (2 × 250 mL) and sodium bicarbonate solution. After the chloroform layer was dried ($MgSO_4$) and the solvent evaporated, the crude product, 4.62 g of a brick-red solid, contained ca. 90% of a material tentatively identified as **4-*tert*-butyl-4,5-dimethoxy-2-hydroxy-2,5-cyclohexadien-1-one.** An analytical sample, appearing as colorless cubes (mp 92–93.5 °C), was obtained by sublimation at 50 °C (0.03 mm) and had the following properties: IR (Nujol) 3380, 1635, 1595, 1355, 1200 cm^{-1}; UV (methanol) λ_{max} 254.4 nm (ϵ 13 552); mass spectrum (CI, methane), *m/e* 227 (MH^+); NMR ($CDCl_3$) δ 6.68 (br s, OH, 1), 5.77 (s, vinyl, 1), 5.72 (s, vinyl, 1),

(11) F. E. Stockelbach, U.S. Patent 2 137 815, 1938.

3.80 (s, CH_3O, 3), 3.10 (s, CH_3O, 3), 0.98 (s, $(CH_3)_3C$, 9).

Anal. ($C_{12}H_{18}O_4$) C, H.

A 2.05-g sample of this 4-*tert*-butyl-4,5-dimethoxy-2-hydroxy-2,5-cyclohexadien-1-one in chloroform was eluted onto 65 g of Brinkmann silica gel, packed in chloroform on a 4-cm-diameter column, and then allowed to stand at room temperature overnight. Slow elution gave 1.70 g of a 70:30 mixture of **5-*tert*-butyl-4-methoxy-1,2-benzoquinone (10)** and the cyclohexadienone. After repetition of the chromatographic process to eliminate methanol, a total of 1.52 g (representing a 71% yield) of bright red, solid *o*-benzoquinone **10** was obtained. Recrystallization from ether at −20 °C provided an analytical sample: mp 95.5–97 °C (large red plates); IR (thin solid film) 1690–1645, 1620 cm^{-1}; UV (methanol) λ_{max} 272.5 nm (ϵ 6540), 417.5 (1100); mass spectrum (CI, ammonia/methane), *m/e* 195 (MH^+); NMR ($CDCl_3$) δ 6.28 (s, CH=, 1), 5.77 (s, C=CO, 1), 3.90 (s, CH_3O, 3), 1.32 (s, $(CH_3)_3C$, 9); ^{13}C NMR ($CDCl_3$) δ 181.59 (s, C=O), 178.73 (s, C=O), 170.68 (s, =$COCH_3$), 159.04 (s, =$CC(CH_3)_3$), 125.72 and 103.41 (2 d, =CH), 56.48 (q, CH_3O), 36.32 (s, $C(CH_3)_3$), 29.66 (q, $(CH_3)_3C$).

Anal. ($C_{11}H_{14}O_3$) C, H.

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Registry No. 1, 67857-70-9; 2, 61186-98-9; 3 (isomer 1), 61186-95-6; 3 (isomer 2), 61186-97-8; **4a**, 1947-24-6; **4b**, 74752-68-4; (*Z,Z*)-**5**, 74752-69-5; (*Z,E*)-**5**, 74752-70-8; **6a**, 74752-71-9; **7a**, 74752-72-0; **7b**, 74752-73-1; 8, 1020-31-1; **10**, 36122-03-9; methoxy(pyridine)copper(II) chloride, 28733-06-4; 4-*tert*-butylcatechol, 98-29-3; 4-*tert*-butyl-1,2-benzoquinone, 1129-21-1; 2-chlorophenol, 95-57-8; 3-chloro-2-hydroxybenzaldehyde, 1927-94-2; 4-*tert*-butyl-4,5-dimethoxy-2-hydroxy-2,5-cyclohexadien-1-one, 74752-74-2.

Direct Optical Resolution of *trans*-1,2-Diaminocyclohexane from an Amine Mixture

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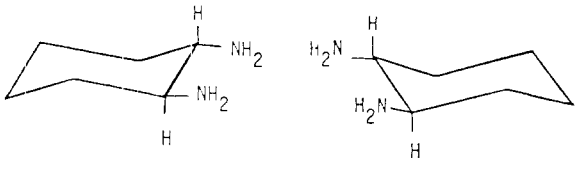
A direct one-step process for the separation and optical resolution of *trans*-1,2-diaminocyclohexane (*trans*-DACH, **1**) from an amine mixture has been developed.[1] *trans*-DACH is the key starting material for the preparation of a variety of optically active alkali metal chelates useful for asymmetric syntheses.[2,3] The process employs a partial molar quantity of natural *d*-tartaric (or *l*-tartaric) acid in combination with a second acid component in an amount sufficient to neutralize all remaining amino groups in the aqueous amine mixture. With *d*-tartaric acid and aqueous propanoic acid, an amine mixture containing 28% **1**, 31% 2-(aminomethyl)cyclopentylamine, and 41% 1,6-hexanediamine gave (*R,R*)-(−)-**1** in 97% optical purity and 99% chemical purity.

As part of a study of the effect of chelating agent structure on the stereoselectivity of the reaction of optically active alkali-metal chelates with prochiral substrates, a facile route to large quantities of (*R,R*)-(−)-**1** and (*S,S*)-(+)-**1** was desired. Racemic *trans*-1,2-cyclohexanediamine



(R,R)-(-)-trans-1 (S,S)-(+)-trans-1

(**1**) is a component in a byproduct amine stream generated during the purification of 1,6-hexanediamine (HDA) which is used in Nylon 66 manufacture. A sample of this byproduct amine stream[4] was N-permethylated[5] and subsequently analyzed by vapor-phase chromatography (VPC). The primary components of this mixture were 31% racemic **1**, 10% 2-(aminomethyl)cyclopentylamine (60% cis, 40% trans), and 51% HDA. The mixture also contained 8% of a fifth component whose structure was not determined. No *meso-cis*-**1** was detected in the mixture.

A variety of inorganic lithium and sodium salts were tried in an effort to effect selective chelate formation with the *trans*-**1** component of the amine mixture.[6] Of the salts tried, LiCl in benzene gave the most selective separation of *trans*-**1** upon recovery of the amine products from the chelate: 86% *trans*-**1** and 14% HDA. This purity was, however, below the 98+% desired, and attention was focused on the direct separation and optical resolution of (*R,R*)-(−)-**1** or (*S,S*)-(+)-**1** from the multicomponent amine mixture.

Optical resolution of *pure trans*-**1** to give (*R,R*)-(−)-**1** has previously been achieved with natural *d*-tartaric acid in aqueous medium.[7] One of the specific properties of *trans*-**1** is its existence as a racemic mixture.[8] Some of the salts of *trans*-**1** also form racemic mixtures. Racemic

(1) T. A. Whitney, U.S. Patent 4 085 138 (1978).
(2) T. A. Whitney and A. W. Langer, *Adv. Chem. Ser.*, **No. 130**, 270 (1974).
(3) T. A. Whitney and A. W. Langer, U.S. Patent 4 156 300 (1979).
(4) While the particular byproduct mixture containing **1** used in this investigation is no longer available, a similar commercial amine mixture (**1** content ~10–25%) is available from Monsanto Chemical Intermediates Co. Also more concentrated **1** of ~60–90% purity is available from Adams Chemical Co, Pfaltz and Bauer, Inc., and Sapon Laboratories. These amine mixtures containing more or less **1** would be treated as described above. The mole fraction of *trans*-**1** is determined, and 1 equiv of *d*- or *l*-tartaric acid is used together with a sufficient quantity of acetic acid, etc. to neutralize all other amino groups in the mixture.
(5) H. T. Clark, H. B. Gillespie, and S. Z. Weisshaus, *J. Am. Chem. Soc.*, **55**, 4571 (1933).
(6) A. W. Langer and T. A. Whitney, U.S. Patent 3 880 925 (1975).
(7) F. M. Jaeger and L. Bijkerk, *Proc. K. Med. Akad. Wet,*, **40**, 12 (1937). R. G. Asperger and C. F. Liu, *Inorg. Chem.*, **4**, 1492 (1965).
(8) For a general reference on racemic modifications, see E. L. Eliel, "Stereochemistry of Carbon Compounds", McGraw-Hill, New York, 1962, Chapter 4.

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