

Crystal Structure of a Tricyclic Product from the Oxidation of 4,5,6-Trichloroguaiacol with Periodate

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(*RS*)-2,3,4',5',6'-Pentachloro-5-methoxy-1',3'-dioxaspiro[cyclohexadiene-1,2-indan]-4-one **2** has been synthesized via oxidative coupling of 4,5,6-trichloroguaiacol caused by periodic acid. The initial coupling step most probably involves the periodic ester of trichloroguaiacol or the corresponding phenoxonium ion. The primary reaction product with the trichlorocatechol formed, is stabilized by spirocyclisation to **2**.

The crystal and molecular structure of **2**, C₁₃H₅Cl₅O₄, were determined by single-crystal X-ray diffraction methods. The compound crystallizes in the space group *P*-1(2) with the following cell dimensions: *a* = 9.386(5) Å, *b* = 12.028(6) Å, *c* = 14.497(10) Å, α = 68.94(4)°, β = 88.24(3)°, γ = 77.52(3)°. The asymmetric unit consists of two virtually identical molecules of **2**. The structure was determined by direct methods and the obtained model containing a total of 397 parameters was refined by full-matrix least-squares calculations that gave a final conventional *R* value of 0.042 for 3407 unique reflections with $I/\sigma(I) \geq 3$.

¹H and ¹³C NMR, IR, UV and mass spectra of **2** are all in accordance with the given structure.

Effluents from the chlorine bleaching of pulp contain a number of chlorinated phenols, catechols and guaiacols.¹ Such effluents also contain very low levels of chlorinated dimers such as dibenzo-*p*-dioxins, dibenzofurans,² alkyldibenzofurans³ and alkylbibenzyls.⁴ Dimers from chlorinated guaiacols have been searched for in the effluents but so far only inconclusive mass spectrometric evidence for their occurrence has been obtained.⁵

Experiments were initiated to prepare such dimers through oxidative coupling of 4,5,6-trichloroguaiacol. Although resistant to oxidation with iron(III) or hexacyanoferrate(III) ions, this phenol gave **1** in a high yield on oxidation in 0.2 mM aqueous solution with the one-electron oxidant iron(III) hexacyanoferrate(III).^{6,7} The formation of **1** was interpreted as proceeding via an oxidative demethylation of trichloroguaiacol through two one-electron steps to 3,4,5-trichloro-*o*-quinone, in a final step rapidly reacting with unchanged guaiacol.

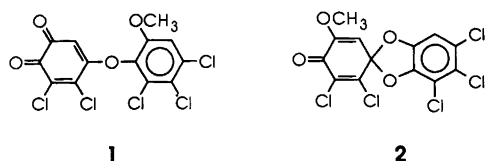
In the present investigation comparative studies were performed using periodate as a two-electron oxidant known to transform guaiacols into *o*-quinones.⁸ Also in

this case **1** was formed as the major product. Unexpectedly, however, it was accompanied by moderate yields of an isomeric, markedly hydrophobic neutral compound. The isomer was ascribed the spirocyclohexadienone-1,2'-dioxaindane structure **2** from X-ray crystallographic studies. ¹H and ¹³C NMR, IR, UV and mass spectra are in accordance with structure **2**.

Experimental

Chemicals. 4,5,6-Trichloroguaiacol was synthesized and purified as described⁹ and was $\geq 99\%$ pure as determined by GLC-FID. Chemicals and solvents were of analytical grade. Thin layer chromatography (TLC) was performed with chloroform as the mobile phase on Merck DC-Fertigplatten Kieselgel 60 F 254 (*R_f*-values: **1** 0.44; **2** 0.72) or with methanol-water (9 : 1 v/v) on Merck Reversed-Phase DC-Fertigplatten RP-18 F 254 S (*R_f*-values: **1** 0.29; **2** 0.33). Column chromatography was run on Merck Kieselgel 60, <0.063 mm.

Instruments. Gas liquid chromatography (GLC) was performed on a DB-5 fused silica capillary column, 30 m × 0.25 mm, 0.025 mm film thickness (J & W Scientific; Folsom CA, USA) and an electron capture detector. Temperature program: 80°C/1 min–30°C/min–240°C–6°C/min–290°C/15 min. The injector and detector tem-



peratures were 210°C and 310°C, respectively. Retention time for **2** 14.40 min; RRT (4,5,6-trichloroguaiacol) 2.13.

Gas liquid chromatography–mass spectrometry (GLC–MS) analysis in the electron impact mode was performed on a Finnigan 4021 instrument upgraded with a 4500 ion source using a GLC column as described above.

¹H and ¹³C NMR spectra were recorded with a JEOL GSX270 instrument. The IR spectrum was recorded on a Perkin-Elmer FT-IR 1725X instrument.

The crystallographic investigations were performed on a Siemens STOE/AED2 diffractometer equipped with a graphite monochromator set to reflect Cu K_α radiation.

(RS)-2,3,4',5',6'-Pentachloro-5-methoxy-1',3'-dioxaspiro[cyclohexadiene-1,2'-indan]-4-one **2**. 4,5,6-Trichloroguaiacol (500 mg, 2.2 mmol) was dissolved in water (5000 ml) at 80°C. Sulfuric acid (9 M) was added to give pH ca. 1, followed by periodic acid (765 mg, 3.3 mmol) with vigorous stirring. After 5 min, the solution was allowed to cool to ambient temperature. Extraction with hexane (2 × 200 ml) gave a product (74 mg) containing **1** and the spiro compound **2** in relative amounts of ca. 2 : 1 as determined by TLC. The identity of **1** was confirmed by reduction with ascorbic acid and methylation of a small sample and comparison with the authentic substance as described.⁶ Compound **2** was not reduced by ascorbic acid. Preparative isolation of **2** was performed through chromatography of the above product on a short silica gel column with dichloromethane as the mobile phase; yield 25 mg (6%) as pale yellow crystals from acetone; m.p. 192–194°C. Found: C 38.3; H 1.3; O 17.1. Calc. for C₁₃H₅Cl₅O₄: C 38.8; H 1.3; O 15.9. MS (IP 70 eV, *m/z*, % rel. intensity): 400 (20, *M*⁺), 365 (100), 302 (80). ¹H NMR (270 MHz, CDCl₃): δ 3.80 (3 H, s), 5.88 (1 H, s),

6.97 (1 H, s). ¹³C NMR (270 MHz, CDCl₃): δ 56.3, 106.3, 108.9, 110.6, 114.7, 124.9, 126.5, 132.7, 143.8, 144.1, 146.0, 151.0, 171.4. IR (KBr): 1713 (s), 1661 (s), 1609 (s), 1460 (s), 1093 (s) cm⁻¹. UV [hexane–ether 4 : 1 (log ε)]: 252 (4.3), 294 (3.7) nm.

Crystallography. Crystal forms of **2** were formed by recrystallisation from acetone. Lattice parameters were refined from 2θ-values of 20 selected reflections. Crystal data are given in Table 1. The background was measured at each end of the scan-interval. Three standard reflections measured every 90 min during the data-collection showed no sign of crystal deterioration. The data were corrected for Lorentz and polarisation effects and also for

Table 2. Fractional atomic coordinates, estimated standard deviations given in parentheses and $U_{eq}/\text{Å}^2$.^a

Atom	<i>x</i>	<i>y</i>	<i>z</i>	U_{eq}
C11A	0.2798(1)	0.3475(1)	0.0980(1)	0.0378(5)
C12A	0.5377(2)	0.3366(1)	0.2349(1)	0.0438(5)
C13A	0.1359(1)	0.5971(1)	-0.0688(1)	0.0382(5)
C14A	0.1058(1)	1.1905(1)	-0.0012(1)	0.0431(6)
C15A	0.1660(2)	0.9015(1)	0.1073(1)	0.0461(6)
O1A	0.4584(4)	0.8019(3)	0.0421(3)	0.0368(13)
O2A	0.2693(4)	0.8079(3)	-0.0613(2)	0.0332(12)
O3A	0.2665(4)	1.2578(3)	-0.1792(3)	0.0380(13)
O4A	0.4746(4)	1.1290(3)	-0.2475(3)	0.0448(15)
C1A	0.3404(5)	0.4788(4)	0.0842(4)	0.0275(16)
C2A	0.2711(5)	0.5888(4)	0.0118(4)	0.0285(17)
C3A	0.3200(5)	0.6910(4)	0.0048(3)	0.0271(16)
C4A	0.4303(5)	0.6863(4)	0.0663(4)	0.0301(17)
C5A	0.5021(5)	0.5801(4)	0.1384(4)	0.0313(18)
C6A	0.4517(5)	0.4753(4)	0.1452(4)	0.0304(17)
C7A	0.3524(5)	0.8852(4)	-0.0369(3)	0.0298(17)
C8A	0.4324(5)	0.9436(4)	-0.1250(4)	0.0316(18)
C9A	0.4080(5)	1.0648(4)	-0.1691(3)	0.0300(18)
C10A	0.2965(5)	1.1487(4)	-0.1352(3)	0.0265(16)
C11A	0.2240(5)	1.0912(4)	-0.0435(3)	0.0256(16)
C12A	0.2487(5)	0.9709(4)	0.0014(3)	0.0286(17)
C13A	0.5899(6)	1.0586(7)	-0.2851(5)	0.0573(30)
C11B	0.1879(2)	1.1630(1)	0.3736(1)	0.0436(5)
C12B	0.3294(1)	0.9611(1)	0.5744(1)	0.0448(5)
C13B	-0.0322(2)	1.1019(1)	0.2473(1)	0.0413(5)
C14B	0.0372(2)	0.4692(1)	0.2516(1)	0.0568(6)
C15B	0.2052(2)	0.6385(1)	0.3121(1)	0.0479(5)
O1B	0.0571(4)	0.6817(3)	0.4861(2)	0.0320(12)
O2B	-0.0527(4)	0.8308(3)	0.3391(2)	0.0329(12)
O3B	-0.2537(4)	0.4769(3)	0.3306(3)	0.0481(16)
O4B	-0.3849(4)	0.5874(3)	0.4483(3)	0.0497(17)
C1B	0.1491(5)	1.0189(4)	0.4145(4)	0.0288(17)
C2B	0.0535(5)	0.9941(4)	0.3544(3)	0.0302(17)
C3B	0.0324(5)	0.8770(4)	0.3855(3)	0.0261(16)
C4B	0.0972(5)	0.7891(4)	0.4723(3)	0.0265(16)
C5B	0.1871(5)	0.8107(4)	0.5346(4)	0.0299(18)
C6B	0.2124(5)	0.9299(4)	0.5011(4)	0.0301(17)
C7B	-0.0391(5)	0.7020(4)	0.4027(3)	0.0280(16)
C8B	-0.1851(5)	0.6844(4)	0.4396(4)	0.0316(18)
C9B	-0.2539(5)	0.6101(4)	0.4177(4)	0.0351(19)
C10B	-0.1889(6)	0.5412(4)	0.3528(4)	0.0340(18)
C11B	-0.0397(6)	0.5532(4)	0.3213(3)	0.0321(17)
C12B	0.0303(5)	0.6248(4)	0.3459(3)	0.0301(17)
C13B	-0.4520(7)	0.6433(6)	0.5164(6)	0.0668(33)

^a $U_{eq} = 1/3 \sum U_{ij}$.

Table 1. Crystal data and data collection parameters.

Compound	C ₁₃ H ₅ Cl ₅ O ₄
Diffractometer	Siemens STOE/AED2
Radiation	Mo K _α (λ = 0.7107 Å)
Space group	<i>P</i> -1 (2)
<i>a</i> /Å	9.386(5)
<i>b</i> /Å	12.028(6)
<i>c</i> /Å	14.497(10)
α/°	68.94(4)
β/°	88.24(3)
γ/°	77.52(3)
<i>V</i> /Å ³	1489(2)
<i>Z</i>	4
<i>F</i> (000)	800
μ(Mo K _α)/cm ⁻¹	9.01
Crystal dimension/mm	0.30 × 0.10 × 0.10
Data collection temperature	293 K
Data collection range	2.0 ≤ 2θ/° ≤ 60
Scan-mode	ω-2θ
Scan-speed/(°s ⁻¹)	0.0075–0.03
Basic scan-width	1.20°
Measured reflections	8570
Observed unique reflections [<i>I</i> > 3σ(<i>I</i>)]	3407
Number of refined parameters	397
Transmission factors	0.820–0.915
$R = \sum F_o - F_c / \sum F_o $	0.042
$R_w = [\sum w(F_o - F_c)^2 / \sum w F_o ^2]^{1/2}$	0.055
Goodness of fit	1.54

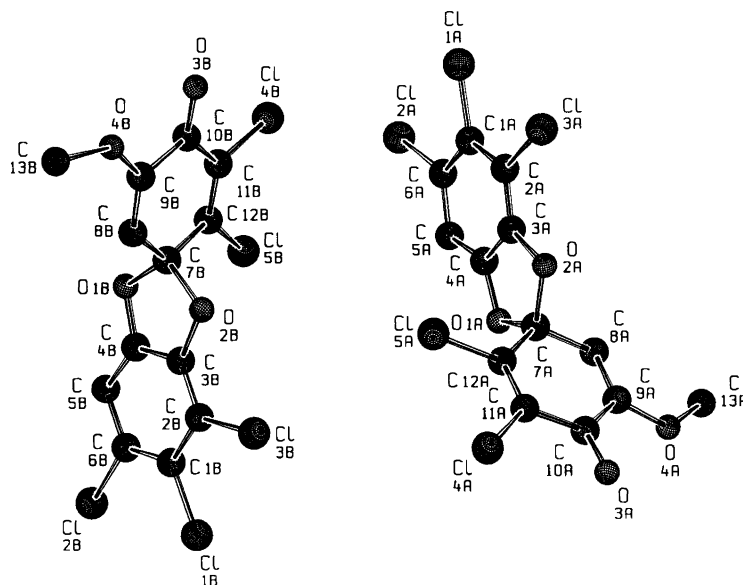


Fig. 1. Numbering scheme of the two independent molecules, *S*-form shown. Hydrogen atoms excluded for clarity.

absorption using numerical integration. The structure was determined by direct methods with the program SHELXS¹⁰ and the model obtained was refined by full-matrix least-squares calculations with the program SHELX.¹¹ The initial model with 177 parameters using isotropic displacement factors for all atoms converged to a conventional *R*-value of 0.122. When anisotropic displacement parameters were used for all non-hydrogen atoms the conventional *R*-value decreased to 0.042.

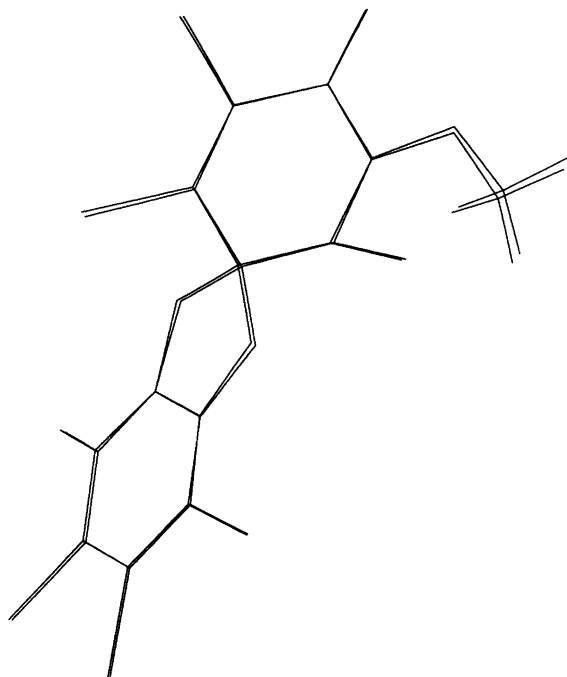
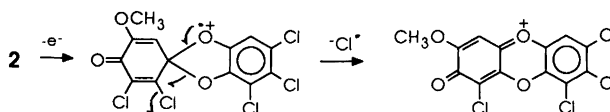


Fig. 2. Superposition of molecule 'A' onto molecule 'B', *S*-form shown.

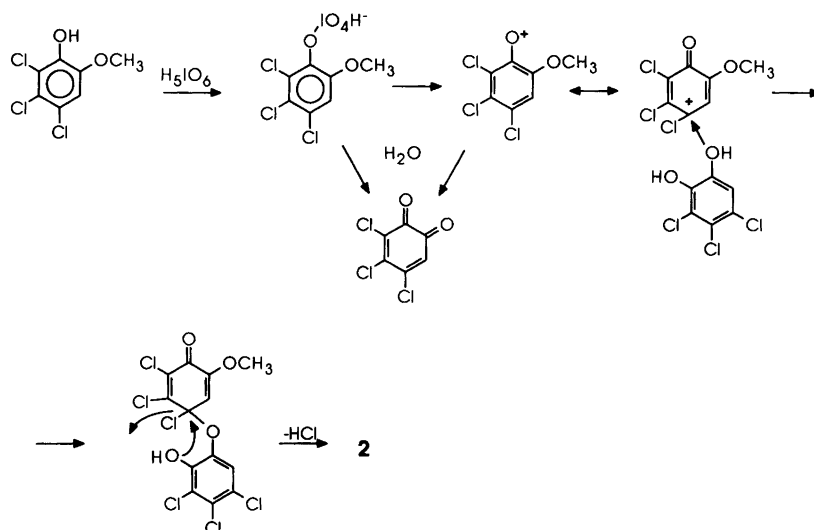
Hydrogen atoms were included in the structure factor calculations but were placed for geometric reasons and given a fixed $U_{\text{iso}} = 0.08 \text{ \AA}^2$. The weighting scheme employed was $w = 1/\{\sigma^2(|F|) + 0.001 \cdot |F|^2\}$ and $\sigma(|F|)$ was determined from counting statistics. In the last cycle there was no change larger than 0.003σ in any of the 397 parameters varied. Fractional atomic coordinates and equivalent isotropic displacement factors are listed in Table 2. The asymmetric unit consists of two stereochemically identical molecules of the title compound, denoted with the letter 'A' or 'B' appended to the atom-names of each molecule. A perspective drawing of the two independent molecules is shown in Fig. 1. The similarity of the two molecules can be seen in Fig. 2. The superposition of molecule 'A' onto molecule 'B' was made with an in-house program¹² implementing the method of Diamond.¹³ The mean distance between corresponding atoms in the superposed molecules is 0.054 \AA with an estimated standard deviation of 0.032 \AA . Both figures were drawn with the program SCHAKAL.¹⁴ A list of geometric parameters and observed and calculated structure factor amplitudes can be obtained upon request from one of the authors (L. Eriksson).

Results and discussion

The crystallographic investigation showed a *p*-quinone monoketal, $\text{C}_{13}\text{H}_5\text{Cl}_5\text{O}_4$, formally derived from two molecules of 4,5,6-trichloroguaiacol. The asymmetric unit contains two identical enantiomers with small conforma-



Scheme 1.



Scheme 2.

tional differences. Since the compound crystallizes well in a centrosymmetric space group equal amounts of both enantiomers are obtained upon crystallization.

The IR spectrum of **2** displays multiple carbonyl bands as reported for 2,5-cyclohexadienones,¹⁵ e.g., *p*-quinone monoketals¹⁵ (cf. Ref. 16 for further references), here influenced with respect to intensity and position by the chlorine substituents. Similarly, the UV spectrum is consistent only with the presence of a cross-conjugated and not with a linearly conjugated cyclohexadienone system.¹⁷

The initial mass fragmentation of **2** on electron impact involves formation of m/z 365 ($M - \text{Cl}$) as the base peak. Most probably, this ion is formed from **2** via ring expansion through a 1,2-shift to give a resonance stabilised oxonium structure (cf. Scheme 1). Further fragmentation through loss of COCl , a characteristic fragmentation pattern of polychlorodibenzo-*p*-dioxins and -furans,¹⁸ would account for the high intensity ion m/z 302.

The formation of **2** can be rationalised as proceeding through two consecutive ionic coupling steps as outlined in Scheme 2. The initial step would involve a labile guaiacol periodic ester or a phenoxonium ion, by analogy with intermediates proposed by Adler *et al.*⁸ in the periodate demethylation of guaiacol to *o*-quinone. Such electrophilic species would be attacked competitively by water, trichlorocatechol and the remaining trichloroguaiacol. The intermediate product thus formed with the catechol is stabilised in a second step by spirocyclisation to **2** with elimination of chloride.

The required trichlorocatechol must derive from the intermediate *o*-quinone, although electron sources for reduction remain undefined (cf. Ref. 19). It is noteworthy that the total recovery of starting material and products was comparatively low. Hence labile degradation products may well account for the reduction of the *o*-quinone.

An alternative coupling mechanism would be oxida-

tion of trichloroguaiacol by formed *o*-quinone. Radical couplings are reported where halogenated quinones function both as electron acceptors and, in reduced form, as coupling partners.^{20,21} Of special interest is the reaction between α -naphthol and tetrachloro-*o*-quinone, where a spiro-type cyclisation product is formed²¹ possibly via two consecutive radical coupling steps. In the present case however, it seems that an analogous route can be excluded since no trace of **2** was detected among products from the reaction of 4,5,6-trichloroguaiacol with preformed *o*-quinone (unpublished results).

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