

(Motherwell, 1978). Compared with the mean values (Table 3), those observed here are normal. We applied the procedure described by Taylor & Kennard (1982), to calculate a standard geometry for the thymine residue (Table 4). Here a standard geometry is defined as one whose bond distances and angles are as close as possible to the average ones observed in crystal structures. Also included in the list are the H atoms, which were calculated with the data from two neutron structures. The use of such standard atomic coordinates has many applications in structural studies of nucleic acids and those for the other bases have already been compiled (Taylor & Kennard, 1982).

Two available protons in the molecule are both involved in intermolecular hydrogen bonds, *i.e.* N(3)—H...O(2) [2.867 (3) Å] and O(3')—H...O(4) [2.817 (3) Å]. The packing scheme in the crystal is shown in Fig. 2.

References

- ALLEN, F. H., BELLARD, S., BRICE, M. D., CARTWRIGHT, B. A., DOUBLEDAY, A., HIGGS, H., HUMMELINK, T., HUMMELINK-PETERS, B. G., KENNARD, O., MOTHERWELL, W. D. S., RODGERS, J. R. & WATSON, D. G. (1979). *Acta Cryst.* **B35**, 2331–2339.
- BECKER, P. J. & COPPENS, P. (1974). *Acta Cryst.* **A30**, 148–153.
- HALL, S. R. & STEWART, J. M. (1987). Editors. *XTAL2.2 User's Manual*. Univ. of Western Australia, Australia, and Maryland, USA.
- KATAHIRA, M., NISHIMURA, Y., TSUBOI, M., SATO, T., MITSUI, Y. & IITAKA, Y. (1986). *Biochim. Biophys. Acta*, **867**, 256–267.
- MOTHERWELL, W. D. S. (1978). *GEOM*. Program for calculating molecular geometry. Univ. of Cambridge, England.
- MOTHERWELL, W. D. S. & CLEGG, W. (1978). *PLUTO*. Program for plotting molecular and crystal structures. Univ. of Cambridge, England.
- NISHIMURA, Y., TSUBOI, M., SATO, T. & AOKI, K. (1986). *J. Mol. Struct.* **146**, 123–153.
- SATO, T. (1983). *Nucleic Acids Res.* **11**, 4933–4938.
- TAYLOR, R. & KENNARD, O. (1982). *J. Am. Chem. Soc.* **104**, 3209–3212.

Acta Cryst. (1988). **C44**, 693–695

Structure of 6-Dodecyl-2-methoxy-1,4-benzoquinone, a New Synthetic Contact Allergen

BY HELMUT W. SCHMALLE

Anorganisch-Chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland

OTTO H. JARCHOW AND GUNADI ADIWIDJAJA

Mineralogisch-Petrographisches Institut der Universität Hamburg, D-2000 Hamburg 13, Federal Republic of Germany

WILFRIED A. KÖNIG, HOLGER HEITSCH AND RALPH RATHMANN

Institut für Organische Chemie der Universität Hamburg, Martin-Luther-King-Platz 6, D-2000 Hamburg 13, Federal Republic of Germany

AND BJÖRN M. HAUSEN AND KARL-HEINZ SCHULZ

Universitäts-Hautklinik Hamburg Eppendorf, Martinistrasse 52, D-2000 Hamburg 13, Federal Republic of Germany

(Received 6 October 1987; accepted 27 November 1987)

Abstract. C₁₉H₃₀O₃, *M_r* = 306.45, triclinic, $P\bar{1}$, *a* = 5.453 (1), *b* = 5.608 (1), *c* = 30.129 (2) Å, α = 85.85 (1), β = 88.66 (1), γ = 83.02 (1)°, *V* = 912.0 (1) Å³, *Z* = 2, *D_x* = 1.116 Mg m⁻³, Cu K α radiation, λ = 1.5418 Å, μ = 0.548 mm⁻¹, *F*(000) = 336, *T* = 296 K, *R* is 0.040 for 2489 observed unique reflections. The aliphatic side chain is slightly rotated from the quinone ring. The angle between the quinone-ring plane and the mean dodecyl-chain plane is 20.8 (2)°. The average C_{sp²}—C_{sp³} bond lengths and

corresponding angles of the side chain are 1.515 (5) Å and 113.8 (3)°. The average dimensions of the quinone ring are C—C 1.477 (4), C=C 1.337 (4), C=O 1.222 (3) Å, C—C—C 118.9 (3), C=C—C 120.6 (3), O=C—C 120.6 (3)°. Neighbouring molecules form dimers by C—H...O interactions across centres of symmetry [C(3)...O(3) 3.413 (2) Å]. The dimers are linked together *via* methyl H and carbonyl O along [100] [C(19)...O(3) 3.338 (3) Å]; O(3) is a bifurcated acceptor.

0108-2701/88/040693-03\$03.00

© 1988 International Union of Crystallography

Introduction. Naturally occurring phenolic and quinonoid compounds are known for their toxic, irritant and allergic properties (Hausen, 1981). 2-Methoxy-6-pentyl-1,4-benzoquinone (primin from *Primula obconica* ssp.) is an example of this class. It is known for its strong sensitizing power (Hjorth, Fregert & Schildknecht, 1969). The allergenic compounds of poison ivy and poison oak (urushiols) are 3-*n*-pentadecylcatechols with an *unsaturated* side chain. They are known to be the most potent sensitizers found in the plant kingdom. Air oxidation or enzymatic oxidation of catechols in the skin to the corresponding *o*-benzoquinone is assumed before covalent binding to a receptor protein of epidermal cells can take place (Byck & Dawson, 1968). Among synthesized 3-*n*-alkylcatechols bearing *saturated* side chains of different lengths (alkyl: C₁ to C₁₉), the optimum of sensitizing power was observed with undecylcatechol (Kurtz & Dawson, 1971). To compare these findings with *p*-benzoquinones, primin analogues (alkyl: C₁ to C₁₅) were synthesized and tested for their allergenic potency (Hausen, Schmalte, Schulz, Faasch, Heitsch, Rathmann & König, 1988). The maximum of allergenicity was reached by a *p*-benzoquinone with a side chain of C₁₁H₂₃. As the urushiols are not available as crystalline samples, X-ray structure analyses of primin analogues have been performed in order to study the properties of *p*-benzoquinonoid allergens with longer side chains. Crystallization experiments were successful for 2-methoxy-6-nonyl-1,4-benzoquinone (Ulrich, Schmalte, Jarchow, König, Heitsch, Rathmann, Hausen & Schulz, 1988) and for the title compound. Contrary to nomenclature rules, the numbering scheme for the quinone ring of the title compound has been chosen for comparison of structural details with other 2-methoxy-6-alkyl-1,4-benzoquinones.

Experimental. The title compound has been prepared by a synthesis described by Schildknecht & Schmidt (1967). Starting with 2-hydroxy-3-methoxybenzaldehyde, the product of the Grignard reaction of this aldehyde with undecylmagnesium iodide was catalytically reduced with H₂/Pd. The 2-dodecyl-6-methoxyphenol obtained was oxidized with potassium-nitrore-disulfonate (Fremy's salt). The 1,4-benzoquinone (m.p. 346 K) was obtained in a yield of 4% after chromatography and crystallization from CHCl₃/hexane.

Very thin yellow platelets were recrystallized from acetone at room temperature. Many trials to cut the crystals for the X-ray experiment to a suitable size of square platelets failed because of the extreme susceptibility and cleavage of the material. The most suitable crystal used for the measurements had approximate dimensions 0.38 × 1.07 × 0.12 mm. Weissenberg and precession photographs showed triclinic symmetry with possible space group *P1* or *P1̄*. Lattice parameters were

determined on an Enraf–Nonius CAD-4 diffractometer with graphite-monochromatized Cu K α radiation, and θ values of 22 reflections in the range $12 < \theta < 42^\circ$ were used for the refinement.

Intensities of 4812 reflections up to $(\sin\theta)/\lambda = 0.588 \text{ \AA}^{-1}$ were recorded using the ω - 2θ scan technique, zigzag mode, and variable scan speeds between 0.27 and 20.0° min⁻¹. The Miller indices ranged: $-6 \leq h \leq 6$, $-6 \leq k \leq 6$, $-35 \leq l \leq 35$. Two standard reflections monitored every 2 h of measuring time showed 0.4% loss of intensities. Four orientation control reflections were measured every 400 recorded data. Data reduction led to 2882 unique reflections, $R_{\text{int}} = 0.018$. L_p and analytical absorption correction were applied, ψ -scan technique, min. and max. transmission factors are 0.8097 and 1.0000. 2489 reflections were considered observed with $I \geq 3\sigma(I)$, 393 reflections were unobserved.

Data statistics showed hypercentricity for this structure, which could be solved by direct methods with *SHELXS84* (Sheldrick, 1984) and subsequent difference Fourier syntheses with *SHELX76* (Sheldrick, 1976), and finally refined by full-matrix least squares minimizing $\sum w(F_o - F_c)^2$, $w = 1/\sigma^2$ on F_{hkl} with anisotropic thermal parameters using the *SDP* program system (Frenz, 1983). All H atoms localized on a difference map and refined isotropically. The refinement of 320 variables and 2489 reflections was stopped at $R = 0.040$ ($wR = 0.036$), $S = 0.377$. The ratio of maximum shift to e.s.d. in final refinement cycle was 0.95 (B_{iso} H atom) and 0.55 (B_{ij} C atom). The maximum height in final difference Fourier synthesis was 0.12 e \AA^{-3} , secondary-extinction value converged at $3.03(4) \times 10^{-6}$. Scattering factors were used as in the *SHELX76* and *SDP* program systems.

Discussion. The final atomic parameters are given in Table 1.* An *ORTEP* view (Johnson, 1971) with atom-numbering scheme, bond distances and angles for non-hydrogen atoms is shown in Fig. 1. The bond lengths and angles are in good agreement with other 2-methoxy-6-alkyl-1,4-benzoquinones (Schmalte, Jarchow, Hausen & Schulz, 1984; Ulrich *et al.*, 1988). The aliphatic side chain is not planar; it is slightly rotated from the quinone-ring plane. The methoxy group, the quinonoid ring, and the dodecyl chain with six groups of three carbon atoms were used for plane calculations. The dihedral angles between the quinone ring and planes are C(6)–C(7)–C(8) 13.4 (2), C(8)–C(9)–C(10) 16.5 (2), C(10)–C(11)–C(12) 19.7 (2),

* Lists of structure factors, anisotropic parameters of the C and O atoms, H-atom coordinates and bond lengths and angles concerning the H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44582 (34 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

C(12)–C(13)–C(14) 22.3 (2), C(14)–C(15)–C(16) 24.3 (2) and C(16)–C(17)–C(18) 28.7 (2)°, the mean angle being 20.8 (2)°. The corresponding angle between the quinone ring and the aliphatic side chain in

2-methoxy-6-pentyl-1,4-benzoquinone is 13.4° (Schmalle *et al.*, 1984), in 2-methoxy-6-nonyl-1,4-benzoquinone 17.4 (3)° (Ulrich *et al.*, 1988).

Table 1. *Positional and equivalent isotropic thermal parameters and their e.s.d.'s*

$$B_{eq} = \frac{1}{3}[a^2B_{11} + b^2B_{22} + c^2B_{33} + ab(\cos\gamma)B_{12} + ac(\cos\beta)B_{13} + bc(\cos\alpha)B_{23}]$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq} (Å ²)
O(1)	0.5484 (3)	0.9791 (3)	0.83900 (5)	5.64 (3)
O(2)	0.5177 (2)	1.2197 (2)	0.91071 (4)	4.75 (3)
O(3)	-0.1394 (3)	0.7829 (2)	0.95770 (4)	5.71 (3)
C(1)	0.3871 (3)	0.9349 (3)	0.86569 (6)	3.86 (4)
C(2)	0.3533 (3)	1.0631 (3)	0.90761 (6)	3.75 (4)
C(3)	0.1780 (3)	1.0162 (3)	0.93782 (6)	4.00 (4)
C(4)	0.0162 (3)	0.8361 (3)	0.92969 (6)	4.14 (4)
C(5)	0.0438 (3)	0.7145 (3)	0.88795 (6)	4.12 (4)
C(6)	0.2186 (3)	0.7535 (3)	0.85756 (6)	3.68 (4)
C(7)	0.2609 (4)	0.6252 (3)	0.81561 (6)	4.36 (4)
C(8)	0.0558 (4)	0.4820 (3)	0.80389 (6)	4.37 (4)
C(9)	0.1072 (4)	0.3518 (3)	0.76144 (6)	4.43 (4)
C(10)	-0.1067 (4)	0.2200 (4)	0.74944 (6)	4.79 (4)
C(11)	-0.0603 (4)	0.0750 (4)	0.70883 (6)	4.66 (4)
C(12)	-0.2796 (4)	-0.0500 (4)	0.69720 (7)	4.95 (4)
C(13)	-0.2357 (4)	-0.2006 (4)	0.65728 (7)	5.02 (5)
C(14)	-0.4577 (4)	-0.3184 (4)	0.64486 (7)	5.31 (5)
C(15)	-0.4127 (4)	-0.4711 (4)	0.60522 (7)	5.47 (5)
C(16)	-0.6364 (4)	-0.5831 (4)	0.59184 (7)	6.02 (5)
C(17)	-0.5870 (5)	-0.7433 (4)	0.55353 (8)	6.89 (6)
C(18)	-0.8126 (5)	-0.8452 (5)	0.53854 (9)	9.12 (7)
C(19)	0.5167 (4)	1.3328 (4)	0.95215 (7)	5.22 (4)

The title compound has a structure similar to those of the most reactive quinonoid allergens known (Kurtz & Dawson, 1971). The sensitizing capacity of substituted *p*-benzoquinones has been discussed elsewhere (Cremer, Hausen & Schmalle, 1987).

Intermolecular distances were calculated up to 3.8 Å with *ORFFE* (Busing, Martin, Levy, Brown, Johnson & Thiessen, 1971). C–H...O hydrogen bonds (Taylor & Kennard, 1982) are found from dimers with lengths C(3)–H(3) = 1.04 (2), H(3)...O(3) = 2.381 (2), C(3)...O(3) = 3.413 (2) Å, the angle around H(3) being 172 (1)° (symmetry operation: $-x, 2-y, 2-z$). The dimers are linked together by C(19)–H(193)...O(3) contacts with lengths C(19)–H(193) = 0.97 (2), H(193)...O(3) = 2.412 (2), C(19)...O(3) = 3.338 (3) Å; the angle around H(193) is 160 (2)° (symmetry operation: $-1+x, -1+y, z$). O(3) is a bifurcated acceptor (Fig. 2).

These investigations were supported by a grant from the Deutsche Forschungsgemeinschaft, Bonn, Federal Republic of Germany.

References

- BUSING, W. R., MARTIN, K. O., LEVY, H. A., BROWN, G. M., JOHNSON, C. K. & THIESSEN, W. E. (1971). *ORFFE*. Oak Ridge National Laboratory, Tennessee, USA.
- BYCK, J. S. & DAWSON, C. R. (1968). *Anal. Biochem.* **25**, 123–135.
- CREMER, D., HAUSEN, B. M. & SCHMALLE, H. W. (1987). *J. Med. Chem.* **30**, 1678–1681.
- FRENZ, B. A. (1983). *Enraf-Nonius Structure Determination Package. SDP Users Guide*. Version of April 1983. Enraf-Nonius, Delft, The Netherlands.
- HAUSEN, B. M. (1981). *Woods Injurious to Human Health*. Berlin, New York: W. de Gruyter.
- HAUSEN, B. M., SCHMALLE, H. W., SCHULZ, K. H., FAASCH, H., HEITSCH, H., RATHMANN, R. & KÖNIG, W. A. (1988). In preparation.
- HJORTH, N., FREGERT, S. & SCHILDKNECHT, H. (1969). *Acta Dermatol. Venerol.* **49**, 552–555.
- JOHNSON, C. K. (1971). *ORTEP*. Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee, USA.
- KURTZ, A. P. & DAWSON, C. R. (1971). *J. Med. Chem.* **14**, 729–732.
- SCHILDKNECHT, H. & SCHMIDT, H. (1967). *Z. Naturforsch. Teil B*, **22**, 287–294.
- SCHMALLE, H. W., JARCHOW, O. H., HAUSEN, B. M. & SCHULZ, K. H. (1984). *Acta Cryst.* **C40**, 1084–1087.
- SHELDRIK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
- SHELDRIK, G. M. (1984). *SHELXS84*. Program for crystal structure solution. Univ. of Göttingen, Federal Republic of Germany.
- TAYLOR, R. & KENNARD, O. (1982). *J. Am. Chem. Soc.* **104**, 5063–5070.
- ULRICH, G., SCHMALLE, H. W., JARCHOW, O. H., KÖNIG, W. A., HEITSCH, H., RATHMANN, R., HAUSEN, B. M. & SCHULZ, K. H. (1988). In preparation.

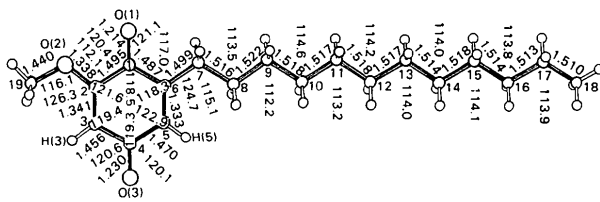


Fig. 1. *ORTEP* drawing of 6-dodecyl-2-methoxy-1,4-benzoquinone with numbering of non-hydrogen atoms and bond distances (Å) and angles (°). The standard deviations of the distances and angles range from 0.003 to 0.006 Å and 0.3 to 0.5° respectively.

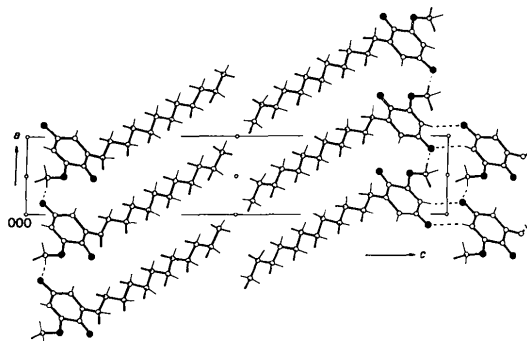


Fig. 2. The *ac* projection of the unit cell showing the chain packing of the molecules. The C–H...O interactions between the quinonoid ring systems are drawn as broken lines. Filled circles of the molecular models indicate O atoms and open circles C atoms.