hydrogen bond between the quinoline N(1) proton and the carbonyl O atom of the amide (McKenna, Beveridge, Jenkins, Neidle & Denny, 1989). In the present case the carboxamide side chain is again oriented so as to form a strong intramolecular hydrogen bond between N(10) and the carbonyl O atom [H(N10)···O(1′) 1.94, N(10)···O(1′) 2.62 Å, N(10)—H(N10)···O(1′) 126.7°]. The amide is essentially coplanar with the C(1)→C(4), C(4a), C(9a) aromatic ring.

References

ATWELL, G. J., CAIN, B. F., BAGULEY, B. C., FINLAY, G. J. & DENNY, W. A. (1984). *J. Med. Chem.* **27**, 1481–1495.

BELL, J. D., BLOUNT, J. F., BRISCOE, O. V. & FREEMAN, H. C. (1968). *Chem. Commun.* pp. 1656–1657.

Enraf–Nonius (1981). *Structure Determination Package*. Enraf–Nonius, Delft, The Netherlands.

HUDSON, B. D., KURODA, R., DENNY, W. A. & NEIDLE, S. (1987). *J. Biomol. Struct. Dyn.* **5**, 145–158.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

McDOWELL, J. J. H. (1969). *Acta Cryst.* B**25**, 2175–2181.

McDOWELL, J. J. H. (1976). *Acta Cryst.* B**32**, 5–10.

McKENNA, R., BEVERIDGE, A. J., JENKINS, T. C., NEIDLE, S. & DENNY, W. A. (1989). *Mol. Pharmacol*, **35**, 720–728.

PALMER, B. D., REWCASTLE, G. W., ATWELL, G. J., BAGULEY, B. C. & DENNY, W. A. (1988). *J. Med. Chem.* **31**, 707–712.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

SHELDRICK, G. M. (1986). *SHELXS*86. Program for the solution of crystal structures. Univ. of Göttingen, Germany.

Acta Cryst. (1992). C**48**, 2007–2009

Structure of the 1:2 Adduct of *meso*-2,3-Dimercaptosuccinic Acid and *N,N*-Dimethylformamide

BY GLORIA J. PYRKA, NELSON SCOTT AND QUINTUS FERNANDO

Department of Chemistry, University of Arizona, Tucson, Arizona 85721, *USA*

(*Received* 15 *October* 1991; *accepted* 4 *March* 1992)

Abstract. $C_4H_6O_4S_2.2C_3H_7NO$, $M_r = 328.20$, monoclinic, $P2_1/c$, $a = 6.408$ (1), $b = 10.433$ (1), $c = 12.388$ (1) Å, $\beta = 98.60$ (1)°, $V = 818.9$ (2) Å^3, $Z = 2$, $D_x = 1.33$ g cm^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 3.3$ cm^{-1}, $F(000) = 348$, $T = 297$ (1) K, $R = 0.041$ for 1006 independent reflections. The C—S bond distance is 1.839 Å. The *meso*-2,3-dimercaptosuccinic acid molecule crystallizes in a staggered configuration with one dimethylformamide molecule hydrogen bonded to each of the carboxylic acid groups.

Introduction. In the 1940's, the dithiol 2,3-dimercapto-1-propanol (British Anti-Lewisite, BAL), was used successfully as an antidote for arsenic poisoning (Peters, Stocken & Thompson, 1945). The effectiveness of BAL in treating poisoning by other heavy metals was tempered by undesirable side effects. The water soluble dithiol 2,3-dimercaptopropanesulfonic acid (DMPS) was synthesized by Petrunkin in the 1950's, and is still the drug of choice for heavy-metal poisoning in the CSR (Petrunkin, 1956). Subsequently, other dithiols have been investigated, *e.g.* *meso*-2,3-dimercaptosuccinic acid (DMSA) (Liang, Chu, Tsen & Ting, 1957) and *N*-(2,3-dimercaptopropyl)phthalamidic acid (Yonaga & Morita, 1981). The dithiol DMSA has been recently approved by the US Food and Drug Administration for the treatment of heavy-metal poisoning.

No structural data are available for any of the dithiols; however, the structure of the monothiol detoxifying agent, 2-amino-3-mercapto-3-methylbutanoic acid (penicillamine) (Rao, Parthasarathy & Cole, 1973), and the structures of several mercury and methylmercury complexes have been determined (Wong, Chieh & Carty, 1973). We report below the structure of the detoxifying agent DMSA, which has been determined as its DMF adduct.

Experimental. Single crystals of the dimercaptosuccinic acid (DMSA)–dimethylformamide (DMF) adduct were produced by cooling a solution of dimercaptosuccinic acid in dimethylformamide. A colorless prism with approximate dimensions 0.27 × 0.33 × 0.50 mm was mounted on a Nicolet/Syntex $P2_1$ diffractometer. The cell constants were determined from 23 reflections in the range $20 < 2\theta < 30°$. The space group was determined to be $P2_1/c$ on the basis of the systematic absences. The $2\theta/\theta$-scan method with a variable scan rate from 2 to 8° min^{-1} (2θ) ($h = 0$ to 7, $k = 0$ to 12, $l = -14$ to 13) was used to collect the data. Three standard reflections, collected after every 96 reflections, decayed by

0108-2701/92/112007-03$06.00

Table 1. *Positional parameters and equivalent isotropic thermal parameters* (Å^2) *for the* 1:2 *DMSA/DMF adduct*

$$B_{eq} = 8\pi^2(U_{11} + U_{22} + U_{33})/3.$$

	x	y	z	B_{eq}
S	0.6745 (1)	0.12655 (8)	0.40058 (7)	5.10 (2)
O1	0.5448 (3)	−0.1995 (2)	0.3426 (2)	4.74 (4)
O2	0.7929 (3)	−0.1631 (2)	0.4846 (2)	5.01 (5)
C1	0.5193 (4)	−0.0083 (3)	0.4419 (2)	3.82 (5)
C2	0.6328 (4)	−0.1324 (3)	0.4266 (2)	3.69 (6)
O3	0.7564 (3)	−0.0968 (2)	0.8121 (2)	4.82 (5)
N	1.0638 (3)	0.0112 (2)	0.8502 (2)	3.71 (5)
C3	0.9412 (4)	−0.0887 (3)	0.8563 (2)	4.09 (6)
C4	1.2838 (5)	0.0112 (3)	0.8983 (3)	5.50 (8)
C5	0.9842 (5)	0.1228 (3)	0.7879 (3)	5.28 (7)

Table 2. *Bond lengths* (Å), *bond angles* (°) *and torsion angles* (°) *for the* 1:2 *DMSA/DMF adduct*

S—C1	1.839 (3)	C1—H1	1.038 (2)
S—HS	1.1058 (7)	O3—C3	1.231 (3)
O1—C2	1.310 (3)	N—C3	1.314 (4)
O1—HO1	0.990 (2)	N—C4	1.446 (4)
O2—C2	1.205 (3)	N—C5	1.447 (4)
C1—C1′	1.507 (4)	C3—H3	1.100 (3)
C1—C2	1.511 (4)	O3—HO1	1.591 (2)

C1—S—HS	103.2 (1)	O1—C2—C1	113.6 (2)
C2—O1—HO1	111.4 (2)	O2—C2—C1	122.4 (2)
S—C1—C1′	110.5 (2)	C3—N—C4	122.0 (2)
S—C1—C2	109.3 (2)	C3—N—C5	120.2 (2)
S—C1—H1	103.0 (2)	C4—N—C5	117.6 (2)
C1′—C1—C2	111.7 (2)	O3—C3—N	125.7 (3)
C1′—C1—H1	110.0 (2)	O3—C3—H3	125.8 (3)
C2—C1—H1	112.0 (2)	N—C3—H3	107.1 (2)
O1—C2—O2	124.0 (3)	O1—HO1—O3	176.0 (2)

HS—S—C1—C2	−50.92 (0.18)	H1—C1—C2—O1	7.22 (0.34)
HS—S—C1—H1	−170.13 (0.16)	H1—C1—C2—O2	−175.21 (0.25)
HS—S—C1—C1′	72.37 (0.19)	C1′—C1—C2—O1	131.13 (0.24)
HO1—O1—C2—O2	1.12 (0.39)	C1′—C1—C2—O2	−51.30 (0.36)
HO1—O1—C2—C1	178.65 (0.21)	S—C1—C1′—C2′	58.11 (0.25)
S—C1—C2—O1	−106.26 (0.23)	S—C1—C1′—H1′	−66.90 (0.29)
S—C1—C2—O2	71.31 (0.30)	C2—C1—C1′—H1′	54.99 (0.33)

less than 4.5%. The linear absorption coefficient was 3.3 cm^{-1}. The data were corrected for Lorentz and polarization factors. 1600 reflections with $2\theta < 50°$ were measured of which 1302 were unique. Intensities of equivalent reflections were averaged; 12 reflections were rejected from the averaging process. The agreement factors for the averaging of the 211 observed and accepted reflections was 0.9% based on intensity and 0.9% based on F_o. The structure was solved by direct methods using *MULTAN* (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982); the positions of all the non-H atoms were located. The H atoms on S, O(1), C(1) and C(3) were found with difference maps and were constrained to the atoms to which they were bonded. The H atoms on the two methyl groups were calculated assuming a bond length of 0.95 Å and regular tetrahedral angles. The orientation of the methyl group was fixed by using one H atom found in the difference map to calculate the remaining two H-atom positions. The H-atom coordinates were not refined. 1006 reflections with intensities greater than $3\sigma(I)$ were used in a full-matrix least-squares refinement of 91 parameters where $\sum w(|F_o| - |F_c|)$ was minimized; w was calculated from $w = 4F/\sigma^2(F^2)$. The refinement converged with $R = 0.041$ and $wR = 0.053$. The ratio of Δ_{max}/σ was 0.02 and the largest peak in the Fourier difference map was 0.33 (4) e Å^{-3}. The scattering factors used were from Cromer & Waber (1974), and anomalous-dispersion effects were included in the values of F_c; the values of f' and f'' were from Cromer (1974). No absorption corrections were employed. All calculations were performed on a PDP-11 computer with the software package *SDP-Plus* (Frenz, 1983).

Discussion. Table 1 contains the final positional and isotropic thermal parameters.* The bond lengths and angles with estimated standard deviations are in Table 2, along with the important torsion angles. The shortest H···O distance is included in Table 2. The structure of dimercaptosuccinic acid is shown in Fig. 1 in an *ORTEP* drawing (Johnson, 1976) with 50% thermal ellipsoids, and a stereoview of the unit cell is shown in Fig. 2. One half of the DMSA and one DMF comprise the unique portion of the cell, with the adduct located on an inversion center. The carboxylic acid group is planar with the largest deviation from the plane being 0.012 Å for C2. The C1—S—HS bond angle is 103.2°. The DMF molecu-

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55279 (12 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: CR0404]

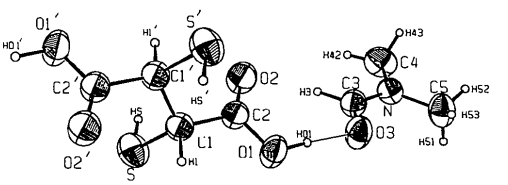


Fig. 1. Molecular geometry of the adduct of *meso*-2,3-dimercaptosuccinic acid with dimethylformamide. The ellipsoids are at the 50% probability level.

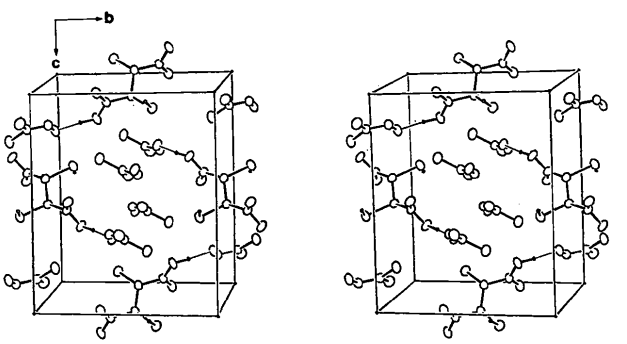


Fig. 2. Stereoscopic view of the unit cell with the 1:2 adduct of DMSA and DMF. The ellipsoids are at the 20% probability level.

lar frame is nearly planar with the largest deviation from the plane being 0.027 Å for N.

The conformation of the *meso* form of DMSA in the solid state is staggered. The two sulfhydryl groups are opposite each other as are the two carboxylic acid groups and the two H atoms. The steric repulsions are minimized by having the bulky carboxylic acid groups between the sulfhydryl group and the H atom. The most notable feature of this adduct is the hydrogen bonding between two dimethylformamide units and the hydroxyl group of the carboxylic acid forming a DMF–DMSA–DMF adduct. The O1—HO1—O3 bond lengths are 0.990 and 1.591 Å, respectively. There are no other unusually short intermolecular contacts.

References

CROMER, D. T. (1974). *International Tables for X-ray Crystallography*, Vol. IV, Table 2.3.1. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

CROMER, D. T. & WABER, J. T. (1974). *International Tables for X-ray Crystallography*, Vol. IV, Table 2.2.B. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

FRENZ, B. A. (1983). *Enraf–Nonius Structure Determination Package*. Version 1.1. Enraf–Nonius, Delft, The Netherlands.

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

LIANG, Y., CHU, C., TSEN, Y. & TING, K. (1957). *Acta Physiol. Sin.* **21**, 24–32.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1982). *MULTAN*11/82. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

PETERS, R. A., STOCKEN, L. A. & THOMPSON, R. H. S. (1945). *Nature (London)*, **156**, 616–619.

PETRUNKIN, V. E. (1956). *Ukr. Khem. Zh.* **22**, 603–607.

RAO, S. N., PARTHASARATHY, R. & COLE, F. E. (1973). *Acta Cryst.* B**29**, 2373–2378.

WONG, Y. S., CHIEH, P. C. & CARTY, A. J. (1973). *Can. J. Chem.* **51**, 2597–2599.

YONAGA, T. & MORITA, K. (1981). *Toxicol. Appl. Pharmacol.* **57**, 197–207.

Acta Cryst. (1992). C**48**, 2009–2013

Structures of Two Crystalline Modifications of Lapachol

BY INGRID KJØLLER LARSEN* AND LISBET AAMAND ANDERSEN

Department of Organic Chemistry, Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen, Denmark

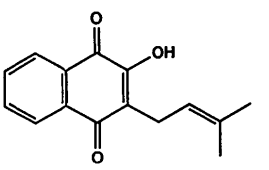
AND BERIT FJÆRTOFT PEDERSEN

Institute of Pharmacy, University of Oslo, N-0315 Oslo, Norway

(*Received* 30 *December* 1991; *accepted* 19 *March* 1992)

Abstract. 2-Hydroxy-3-(3-methyl-2-butenyl)-1,4-naphthalenedione, $C_{15}H_{14}O_3$, $M_r = 242.26$. Triclinic (LAPA I), $P\bar{1}$, $a = 5.960$ (1), $b = 9.569$ (2), $c = 10.679$ (2) Å, $\alpha = 96.82$ (2), $\beta = 98.32$ (2), $\gamma = 90.32$ (2)°, $V = 598.2$ (3) Å^3 at 105 K, $Z = 2$, $D_x = 1.345$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 0.087$ mm^{-1}, $F(000) = 256$, $T = 105$ K, final $R = 0.028$ for 1249 unique observed reflections. Monoclinic (LAPA II), $P2_1/c$, $a = 6.035$ (1), $b = 9.427$ (2), $c = 20.918$ (5) Å, $\beta = 98.27$ (2)°, $V = 1177.7$ (5) Å^3 at 105 K, $Z = 4$, $D_x = 1.366$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 0.088$ mm^{-1}, $F(000) = 512$, $T = 105$ K, final $R = 0.027$ for 739 unique observed reflections. In both crystalline modifications of lapachol the naphthoquinone ring system is approximately planar, and the planar unsaturated side chain is twisted about 90° with respect to the ring system. The crystal packings of LAPA I and II show that the molecules, in both cases, form dimers through OH···O hydrogen bonds around centres of symmetry.

Introduction. Lapachol (LAPA) is a natural pigment derived from the heart wood of certain tropical plants (Hooker, 1896). It has been known for several years that the compound is an active antineoplastic agent (Rao, McBride & Oleson, 1968), but the anticoagulant effects encountered during the clinical testing of lapachol have prevented its use as an



LAPA

* To whom correspondence should be addressed.

0108-2701/92/112009-05$06.00