short. Consequently, the O$\cdots$H distance will be about 0·05 to 0·10 Å too long. Taking this into account, the neutron ('true') asymmetry of the Li salt is expected to be in the order of 0·15 Å, a value close to $\Delta = 0\cdot184$ Å (see Table 2) observed in the neutron analysis of the Ca salt (Hsu & Schlemper, 1980). An asymmetry sequence $\Delta(\text{Li}) \approx \Delta(\text{Ca}) < \Delta(\text{Na})$ may be rationalized in terms of the asymmetry of the surroundings of the HM ion. Fig. 2 depicts the direct environment of HM *inter alia* the three salts. One notes the large asymmetry in the Na salt and the lesser one in the Li and Ca salts, which moreover show a strong mutual resemblance. Evidence, suggesting that the surroundings not only affect the asymmetry of the intramolecular hydrogen bond but also to some extent the geometry of the HM ion itself, can be obtained by comparing the X-ray geometry of the heavy-atom skeleton with the neutron geometry of the Na, Zn, Ca and Mg salts. The comparison is meaningful, because we know from a previous observation in magnesium bis(hydrogen maleate) hexahydrate (Vanhouteghem *et al.*, 1987) and from a statistical study by Allen (1986) that only very small differences exist between neutron and X-ray values of CC and CO lengths. We performed a cluster analysis (*e.g.* Everitt, 1981) on the five salts using the heavy-atom geometry (bond lengths in pm and valence angles in decimal degrees) as the attributes. From the Euclidean metric distance matrix and the nearest-neighbour method the dendrogram of Fig. 3(a) is obtained. The same analysis on the asymmetry parameters gives the dendrogram of Fig. 3(b). There is a distinct similarity. The only difference is that the Zn salt is closer to the Na salt in a hierarchical associative clustering based on bond lengths and angles, whereas it is closer to the Ca salt (see also Fig. 3c) in a clustering based on Δ values. We interpret the similarity to reveal that the asymmetry of the HM surroundings, which

correlates with Δ values (Fig. 2), also correlates with HM geometry.

References

ALLEN, F. H. (1986). *Acta Cryst.* B42, 515–522.
CHIARI, G. & FERRARIS, G. (1982). *Acta Cryst.* B38, 2331–2341.
DARLOW, S. F. & COCHRAN, W. (1961). *Acta Cryst.* 14, 1250–1257.
EVERITT, B. (1981). In *Cluster Analysis*. London: Halsted, Heinemann Press.
FERRARIS, G. & FRANCHINI-ANGELA, M. (1972). *Acta Cryst.* B28, 3572–3583.
FRENZ, B. A. (1978). *Computing in Crystallography*, edited by H. SCHENK, R. OLTHOF-HAZEKAMP, H. VAN KONINGSVELD & G. C. BASSI, pp. 64–71. Delft Univ. Press.
GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A27, 368–376.
GUPTA, M. P., PRASAD, S. M. & GUPTA, T. N. P. (1975). *Acta Cryst.* B31, 37–40.
HSU, B. & SCHLEMPER, E. O. (1980). *Acta Cryst.* B36, 3017–3023.
International Tables for X-ray Crystallography (1974). Vol. IV, pp. 71–98. Birmingham: Kynoch Press. (Present distibutor Kluwer Academic Publishers, Dordrecht.)
OLOVSSON, G., OLOVSSON, I. & LEHMANN, M. S. (1984). *Acta Cryst.* C40, 1521–1526.
SEQUEIRA, A., RAJAGOPAL, H., GUPTA, M. P., VANHOUTEGHEM, F., LENSTRA, A. T. H. & GEISE, H. J. (1989). *Acta Cryst.* Submitted.
VANHOUTEGHEM, F., LENSTRA, A. T. H. & SCHWEISS, P. (1987). *Acta Cryst.* B43, 523–528.

2-(O-Ethyl dithiocarbonato)succinic Acid

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Abstract. $C_7H_{10}O_5S_2$, $M_r = 238\cdot3$, monoclinic, $P2_1/c$, $a = 11\cdot906$ (3), $b = 5\cdot363$ (1), $c = 19\cdot167$ (4) Å, $\beta = 114\cdot71$ (2)°, $V = 1111\cdot8$ (4) Å^3, $Z = 4$, $D_m = 1\cdot420$ (4), $D_x = 1\cdot424$ g cm^{-3}, $\lambda(\text{Mo }K\alpha) = 0\cdot71069$ Å, $\mu = 4\cdot62$ cm^{-1}, $F(000) = 496\cdot9$, $T = 297$ K, $R = 0\cdot0834$, $wR = 0\cdot0510$ for 1326 unique reflections and 127 parameters. The structure is described by the name and bond lengths and angles are normal, although the

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C—S—C angle [105·4 (2)°] is large. The C(thio-formate)—S bond [1·745 (5) Å] is shorter than the C(succinic acid)—S bond [1·831 (4) Å]. The conformation of the molecule is determined by non-bonding repulsions.

Introduction. Thiol complexes of gold and D-penicillamine are used in the treatment of rheumatoid arthritis (Merril, Shaw, Spadaro & Etris, 1987; Howard-Lock, Lock, Mewa & Kean, 1986). Although it is believed that the gold is an important factor in the response, the fact that thiols alone can have similar effects raises questions as to whether gold is acting as an expensive carrier for the thiol ligand. Thus there have been extensive chemical and biochemical studies of the thiol complexes and the thiols themselves. To this end, we have synthesized the O-ethyl thioformate complex of thiomalic acid and determined its structure. The title compound was prepared by the reaction of bromo-succinic acid with O-ethyl dithiocarbonic acid in cold aqueous Na_2CO_3 solution (Biilmann, 1905). Crystals were grown from aqueous solution.

Experimental. Density by suspension in dichloro-methane/chloroform mixture. Crystal chosen for diffraction: parallelepiped, 0·19 × 0·11 × 0·35 mm. Unit-cell parameters refined by least-squares fit of positional angles for 15 strong reflections, $10·4 < 2\theta < 18·3°$, on a Nicolet $P3$ diffractometer, graphite-monochromated Mo $K\alpha$ radiation, 1640 reflections measured for $2\theta < 45°$. Intensities $0 \le h \le 12$, $0 \le k \le 5$, $-15 \le l \le 15$, measured by θ–2θ scan technique. Range of scan rates 4·9 to 29·3° min^{-1} in 2θ. The total background time to scan time ratio is 1:1. Two standard reflections measured every 48 reflections ($0\bar{1}2$, 1·37%; $50\bar{4}$, 1·60%) showed no instrument instability or crystal decay. Zonal reflections averaged to give 1326 independent reflections, $R_{int} = 0·024$. Reflections with $3\sigma_I \ge I \ge -3\sigma_I$ were treated by the method of French & Wilson (1978). Lp corrections were made, but no corrections were made for absorption (absorption correction factors 1·045–1·099 for maximum error in F_o of 1·3%). Structure solved by direct methods based on 359 reflections with $|E| > 1·2$ and 40 sets of starting phases. Anisotropic full-matrix least-squares refinement minimized $\sum w(|F_o| - |F_c|)^2$, $w = (\sigma_F^2 + 0·000103F_o^2)^{-1}$. Scale, positional and anisotropic temperature factors for non-H atoms varied, 127 parameters. H atoms on molecule included but not refined. H atoms on O1 and O4 not found. Final $R = 0·0834$, $wR = 0·0510$, $S = 1·525$. The large value of R is caused by the large number of reflections with $I < 3\sigma_I$. Refinement ended when $(\Delta/\sigma)_{max} = 0·035$. Final difference map revealed electron density max. 0·41 min, −0·40 e Å^{-3}. Scattering factors from Cromer & Waber (1974). Corrections for anomalous dispersion made for S (Cromer & Ibers, 1974). Calcula-

Table 1. *Atomic positional parameters* ($\times 10^4$) *and isotropic temperature factors* (Å$^2 \times 10^3$)

	x	y	z	U_{eq}*
S1	3938 (1)	2 (3)	1804 (1)	35·5
S2	5533 (2)	1803 (5)	1120 (1)	117
C1	1329 (5)	4014 (10)	2236 (3)	32
C2	2419 (4)	3573 (9)	2040 (3)	30
C3	2421 (4)	944 (8)	1741 (3)	28
C4	1368 (4)	534 (10)	952 (3)	34
C5	4171 (5)	1771 (11)	1112 (3)	46
C6	3218 (6)	4499 (16)	29 (4)	91
C7	2070 (8)	4114 (19)	−658 (4)	129
O1	1129 (3)	6380 (6)	2305 (2)	49
O2	736 (3)	2344 (6)	2340 (2)	48
O3	578 (3)	2136 (6)	661 (2)	41
O4	1359 (3)	−1635 (6)	642 (2)	44
O5	3171 (3)	2904 (6)	635 (2)	52

* $U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33} + 2\cos\beta U_{13})$.

Table 2. *Selected interatomic distances* (Å) *and angles* (°)

C1—C2	1·513 (6)	C2—C3	1·523 (6)
C3—C4	1·524 (6)	C3—S1	1·831 (4)
S1—C5	1·745 (5)	C5—O5	1·309 (5)
O5—C6	1·463 (7)	C6—C7	1·462 (9)
C1—O1	1·308 (6)	C1—O2	1·207 (5)
C4—O3	1·223 (5)	C4—O4	1·304 (5)
C5—S2	1·615 (5)		
O1—C1—O2	124·0 (5)	O1—C1—C2	112·8 (4)
O2—C1—C2	123·1 (5)	C1—C2—C3	112·0 (4)
C2—C3—C4	112·2 (4)	C2—C3—S1	112·8 (3)
C3—C4—O3	120·5 (5)	C3—C4—O4	115·4 (4)
O3—C4—O4	124·1 (5)	C3—S1—C5	105·4 (2)
S1—C5—O5	113·3 (4)	S1—C5—S2	118·5 (2)
S2—C5—O5	128·2 (4)	C5—O5—C6	120·0 (4)
O5—C6—C7	107·5 (6)	C4—C3—S1	113·9 (3)

Hydrogen bonds

O2···O1	2·631 (5)	O3···O4	2·610 (5)

tions employed *XTAL* (Stewart & Hall, 1983), *SHELX76* (Sheldrick, 1976), and *SNOOPI* (Davies, 1983) program systems on a VAX 8650 computer. Atomic positional parameters and U_{eq} are given in Table 1.*

Discussion. The molecule is shown in Fig. 1 and bond distances and angles are given in Table 2. Bond lengths and angles are normal. Although the H atoms on the carboxylate groups were not detected, they are clearly attached to O1 and O4 since the C—O(H) [C1—O1, 1·308 (6), C4—O4, 1·304 (5) Å] and C—O [C1—O2, 1·207 (5), C4—O3, 1·223 (5) Å] distances and C—C—O(H) [C2—C1—O1, 112·8 (4), C3—C4—O4,

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* Lists of structure factors, anisotropic temperature factors, H-atom positions, bond lengths and angles involving H atoms, and best planes, dihedral and torsional angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51710 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

115·4 (4)°] and C—C=O [C2—C1—O2, 123·1 (5), C3—C4—O4, 120·5 (5)°] angles agree well with values we have observed previously for sulfur-containing carboxylic acids (Howard-Lock, Lock & Smalley, 1985). The small geometry differences for the two carboxylate groups are related to the strengths of the hydrogen bonds. The C3—S1—C5 angle [105·4 (2)°] is relatively large, probably because of delocalization of double-bond character from C5—S2 into adjacent bonds. Thus C5—S1 [1·745 (5) Å] is significantly shorter than C3—S1 [1·831 (4) Å]. Although we have previously seen asymmetry in two carbon bonds attached to an S atom (Howard-Lock et al., 1985; Howard-Lock, Lock, Martins, Faggiani & Duarte, 1987), the C5—S1 distance lies below the end of the
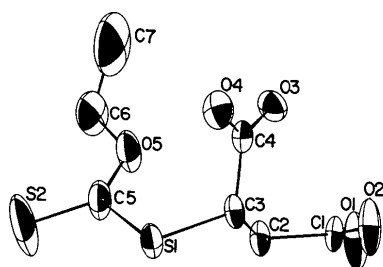

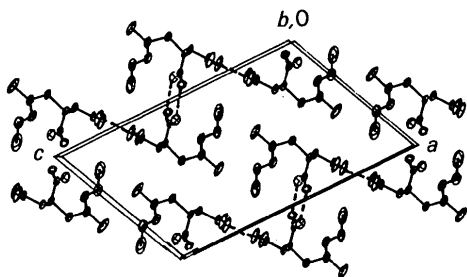Fig. 1. The molecule showing the atom numbering. H atoms are omitted.

Fig. 2. A view down b of the unit-cell packing showing the hydrogen bonding (broken lines), in particular the O3···O4'···O3'···O4 rings.
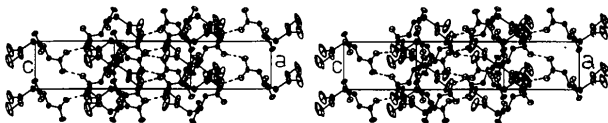

Fig. 3. Stereoview of the packing of the molecule in the unit cell, showing in particular the O1···O2' and O1'···O2'' hydrogen bonds (broken lines). The view is along [201]. The a and c axes, which are parallel to the bottom of the page, have an origin at the vertical b axis near the centres of the diagrams. The directions of the a and c axes are indicated by letters at the vertical edges terminating the axes.

range. However, it is larger than the value for the C*—S* bond in the unit RC = C(SR')—C*(=S)—S*—R'' (1·719 Å, Slot, Kron, Brouwer & Bos, 1981) or the corresponding C—S bond in potassium O-ethyl dithiocarbonate (1·66, 1·71 Å, Mazzi & Tadini, 1963). The general features of the xanthate unit agree reasonably well with those of related structures. Although the C5—O5 distance [1·309 (5) Å] is very short for a single bond (1·43 Å, Pauling, 1960), closer to the double-bond distance (1·287 Å, Pauling, 1960) and shorter than the C—O bond in potassium O-ethyl dithiocarbonate (1·34, 1·36 Å, Mazzi & Tadini, 1963), it is close to the C—N distance in tetramethylthiuram disulfide (1·31 Å, Marov, 1965). This implies considerable delocalization into the C—O bond but, strangely, the C=S bond is not exceptionally long [1·615 (5) Å]. It is shorter than the C=S bond in the O-ethyl dithiocarbonate ion (1·67, 1·69 Å, Mazzi & Tadini, 1963) but comparable to C=S distances in other related molecules (1·61, 1·631, Marov, 1965; Slot et al., 1981). The conformation of the molecule is determined by the need to minimize non-bonding repulsions. The packing is shown in Figs. 2 and 3.

The molecules appear to form layers parallel to the (102) planes, but the dominant feature of the structure is the hydrogen-bonding network between the carboxylate groups within double layers of molecules centred about the a faces. Within a double layer there are two types of hydrogen bonds. Pairs of molecules related by the inversion centres at 0, ½, ½ and 0, 0, 0 are bound across the a face through O4H···O3'/O3···HO4' hydrogen bonds. Along the b direction there are chains of molecules related by the 2₁ axis bound through O1H···O2'/O1'H···O2''/etc. hydrogen bonds. The asymmetric thermal motions of C1, O1 and C2 suggest that the carboxylate group shows a large librational motion out of the C2, C1, O1, O2 plane. The chain-like nature of the O1···O2···O1···O2··· hydrogen bonding imposes fewer restraints than the O3···O4'··· O3'···O4 ring and, although bonds within a given chain will be correlated, there need not be interchain correlation. There is no significant interaction between double layers at 0, ½, 0, except for van der Waals forces, and this lack of constraint permits the large thermal motion of S2 and C6.

References

BIILMANN, E. (1905). Justus Liebigs Ann. Chem. 339, 351–372.
CROMER, D. T. & IBERS, J. A. (1974). International Tables for X-ray Crystallography, Vol. IV, edited by J. A. IBERS & W. C. HAMILTON, Table 2.3.1, pp. 149–150. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

CROMER, D. T. & WABER, J. T. (1974). *International Tables for X-ray Crystallography*, Vol. IV, edited by J. A. IBERS & W. C. HAMILTON, Table 2.2B, pp. 99–101. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

DAVIES, K. (1983). *CHEMGRAF* suite, program *SNOOPI*. Chemical Design Ltd, Oxford, England.

FRENCH, S. & WILSON, K. (1978). *Acta Cryst.* A34, 517–525.

HOWARD-LOCK, H. E., LOCK, C. J. L., MARTINS, M. L., FAGGIANI, R. & DUARTE, M. (1987). *Can. J. Chem.* 65, 878–883.

HOWARD-LOCK, H. E., LOCK, C. J. L., MEWA, A. & KEAN, W. F. (1986). *Semin. Arthritis Rheum.* 15, 261–281.

HOWARD-LOCK, H. E., LOCK, C. J. L. & SMALLEY, P. S. (1985). *Can. J. Chem.* 63, 2411–2419.

MAROV, K. (1965). *Acta Chem. Scand.* 19, 1509.

MAZZI, F. & TADINI, C. (1963). *Z. Kristallogr.* 118, 378–392.

MERRIL, C. R., SHAW, C. F., SPADARO, J. A. & ETRIS, S. F. (1987). In *Proceedings of the First International Conference on Gold and Silver in Medicine*. Washington, DC: The Gold Institute/The Silver Institute.

PAULING, L. (1960). *The Nature of the Chemical Bond*, 3rd ed., pp. 224, 228. Ithaca, NY: Cornell Univ. Press.

SHELDRICK, G. M. (1976). *SHELX76.* Program for crystal structure determination. Univ. of Cambridge, England.

SLOT, H. J. B., KRON, J., BROUWER, A. C. & BOS, H. J. T. (1981). *Acta Cryst.* B37, 1871–1873.

STEWART, J. M. & HALL, S. R. (1983). The *XTAL* system. Tech. Rep. TR-1364. Computer Science Center, Univ. of Maryland, College Park, Maryland, USA.

Structure of a Propynyl Adduct of an Oxa-Bridged Octalin*

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Abstract. $C_{20}H_{30}O_6$, $M_r = 366 \cdot 45$, monoclinic, $P2_1/n$, $a = 10 \cdot 411$ (2), $b = 16 \cdot 084$ (3), $c = 11 \cdot 991$ (1) Å, $\beta = 100 \cdot 98$ (2)°, $V = 1971$ (6) Å^3, $Z = 4$, $D_x = 1 \cdot 23$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0 \cdot 71069$ Å, $\mu = 0 \cdot 097$ mm^{-1}, $F(000) = 792$, $T = 296$ K, $R = 0 \cdot 050$, $wR = 0 \cdot 065$ for 3430 observed unique reflections. The structure of a key synthetic intermediate for use in a total synthesis of the nargenicin antibiotics has been established by X-ray single-crystal methods. Its structure is characterized by an essentially strain-free tricyclic oxa-bridged octalin nucleus, low-energy methoxymethyl ether side-chain conformations and an intramolecular hydrogen bond between the hydroxyl group hydrogen atom and a methoxymethyl ether oxygen atom. Intermolecular packing contacts less than the sum of van der Waals radii consist of weak C—H⋯O interactions.

Introduction. The nargenicins [(1)–(3), Scheme 1] constitute a new structural class of macrolide antibiotics which exhibit significant activity against drug-resistant microorganisms. First isolated by groups at Pfizer (Celmer, Chmurny, Moppett, Ware, Watts & Whipple, 1980) and Upjohn (Whaley, Chidester, Misak & Wnuk, 1980; Magerlein & Reid, 1982), the nargenicins are characterized by the presence of a highly functionalized decanolide system fused to an 11-oxatricyclo[4.4.1.0^{2,7}]undecene nucleus. Studies in our laboratories have focused on the development of an efficient, stereo-controlled route to the nargenicins (Kallmerten, 1984; Kallmerten & Plata, 1987) and have recently culminated in the total synthesis of 18-deoxynargenicin A$_1$, (3) (Plata & Kallmerten, 1988). While our convergent approach to (3) rapidly assembles the key structural elements of the nargenicin macrolide system, it ultimately fails to control stereochemistry at C$_{16}$ and C$_{17}$ (Scheme 1). Consequently, we are investigating an alternative strategy in which the remote stereochemical elements of the macrolide system will be introduced *via* the stereoselective sigmatropic homologation of a tertiary allylic ether.
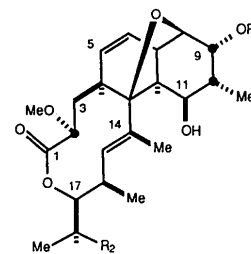
(1) R$_1$= 2-carboxypyrrole, R$_2$= OH, nargenicin A$_1$
(2) R$_1$= H, R$_2$= OH, nodusmicin
(3) R$_1$= 2-carboxypyrrole, R$_2$= H, 18-deoxynargenicin A$_1$

Scheme 1

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*IUPAC name: (2*R**)-2-{(1*R**,5*S**,6*S**,7*S**,8*S**,9*S**,10*R**)-7,9-bis(methoxymethoxy)-8-methyl-11-oxatricyclo[4.4.1.0^{2,7}]undec-2-en-3-yl}-3-pentyn-2-ol.

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