Tetrahedron. Vol 27, pp. 6143–6149. Pergamon Press 1971. Printed in Great Britain

AN UNEXPECTED SPIROCYCLIC PRODUCT FROM THE REACTION OF 3-(3-METHYL-2-OXOBUTYL)-3-HYDROXYOXINDOLE WITH THIONYL CHLORIDE

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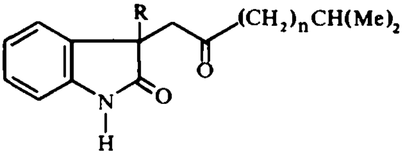
(*Received in the UK* 11 *August* 1971; *Accepted for publication* 18 *August* 1971)

Abstract—Treatment of 3-(3-methyl-2-oxobutyl)-3-hydroxyoxindole with thionyl chloride gives an unexpected product which was shown by single crystal X-ray analysis to be 2-oxoindoline-3-spiro-2'-(3'-chloro-5', 5'-dimethyl-4'-oxothiolane-1'-oxide). The crystals are monoclinic ($P2_1$) with $a = 8{\cdot}324$ $b = 10{\cdot}982$ and $c = 7{\cdot}271$ Å. $\beta = 93{\cdot}12°$. The indole nucleus is not quite planar—the two fused rings are at an angle of 3°.

INTRODUCTION

Compounds of type **1** ($R = OH$, $n < 2$) show asymmetry splitting of the NMR signals from the gem dimethyl group. For a study of the influence of the substituent (R) on this effect a series of compounds of type **1** was needed.



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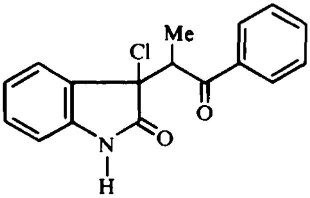

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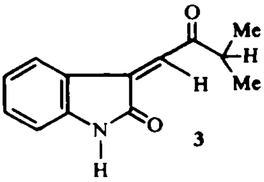
3-(2-Oxoalkyl)-3-hydroxyoxindoles (**1**, $R = OH$) are easily prepared by a Et_2NH catalyzed condensation using isatin and the appropriate methylketone.[1] As Pietra and Tacconi[2] have claimed the formation of **2** from the corresponding 3-hydroxy-compound upon treatment with $SOCl_2$, an analogous substitution of **1** ($R = OH$) seemed plausible.

Treatment of **1** ($R = OH$, $n = 0$) or **3** with $SOCl_2$ gave, however, a product in



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obvious disagreement with the anticipated structure. The elemental analysis and the mass spectrum showed the following composition: $C_{13}H_{12}ClNO_3S$.

As several structures were considered possible even after studying the IR- and NMR-data, an X-ray analysis was undertaken.

Structure determination and refinement of $C_{13}H_{12}ClNO_3S$

The structure was solved by the heavy-atom method. The sulphur and chlorine atoms were located from a three dimensional Patterson map. The y-coordinate for the sulphur atom was arbitrarily given the value 0·25.

A structure factor calculation on these two atoms gave an R-value of 0·39. All non-hydrogen atoms were then found in successive rounds of structure factor and electron density calculations. The atoms were refined with block-diagonal least-squares technique using isotropic temperature factors except for the sulphur and chlorine atoms, which were refined anisotropically. (In the block-diagonal refinement also the sulphur y-coordinate was refined which explains the small deviation from 0·25 in Table 1.)

TABLE 1. FRACTIONAL ATOMIC COORDINATES WITH STANDARD DEVIATIONS ($\times 10^4$) FOR THE NON-HYDROGEN ATOMS OF THE STRUCTURE

		x	$\sigma(x)$	y	$\sigma(y)$	z	$\sigma(z)$
N	(1)	−0·1283	(7)	0·4451	(6)	0·1372	(7)
C	(2)	−0·0022	(8)	0·4287	(6)	0·2610	(7)
C	(3)	0·0104	(6)	0·2896	(4)	0·2890	(6)
C	(4)	−0·1823	(7)	0·1198	(7)	0·1545	(9)
C	(5)	−0·3224	(9)	0·1035	(11)	0·0421	(11)
C	(6)	−0·4006	(9)	0·1981	(15)	−0·0426	(11)
C	(7)	−0·3448	(10)	0·3171	(15)	−0·0221	(9)
C	(8)	−0·2068	(7)	0·3352	(7)	0·0870	(7)
C	(9)	−0·1283	(6)	0·2391	(7)	0·1776	(7)
O	(10)	0·0851	(7)	0·5022	(4)	0·3350	(6)
S	(1′)	0·2081	(1)	0·2486	(-).	0·1864	(1)
C	(3′)	0·0316	(5)	0·2536	(6)	0·4907	(6)
C	(4′)	0·2004	(6)	0·2823	(5)	0·5604	(6)
C	(5′)	0·3229	(6)	0·2596	(6)	0·4130	(7)
Cl	(6′)	0·1130	(2)	0·3177	(2)	0·6262	(2)
O	(7′)	0·2406	(5)	0·3158	(6)	0·7123	(5)
C	(8′)	0·4062	(10)	0·1381	(8)	0·4513	(11)
C	(9′)	0·4400	(10)	0·3643	(9)	0·4078	(11)
O	(10′)	0·1975	(5)	0·1185	(4)	0·1341	(6)

At an R-value of 0·09 the hydrogen atoms were all located from a Fourier difference map. In the final refinement the full matrix was used. All positional parameters were varied as well as anisotropic thermal parameters for all non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms. The final R-value was 0·033 for the 1114 observed independent reflections.

All calculations were performed on a Datasaab D21 computer with the programme system of Abrahamsson *et al.*[3] The formfactors were those given in the International Tables for X-ray Crystallography, Vol. III[4] for the heavier atoms whereas for hydrogen the values given by Stewart, Davidson and Simpson[5] were used.

The weight assigned to each observation in the least-squares refinement was

$$w = \frac{1}{1 + \left(\frac{|Fo|}{6{\cdot}75\,|F_{min}|}\right)^2}$$

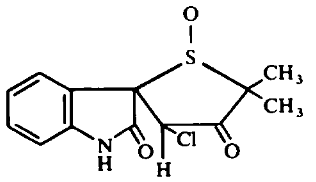
Description of the structure

The final atomic parameters are given in Tables 1, 2 and 3. A list of the observed and calculated structure factors can be obtained from the Crystallography Group.

TABLE 2. ANISOTROPIC THERMAL PARAMETERS IN THE FORM $\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2klb^*c^*U_{23} + 2lha^*c^*U_{31} + 2hka^*b^*U_{12})]$ STANDARD DEVIATIONS ARE GIVEN IN PARENTHESES. ALL VALUES HAVE BEEN MULTIPLIED BY 10^4.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{31}	U_{12}
N (1)	750 (37)	549 (36)	486 (29)	204 (27)	161 (26)	283 (30)
C (2)	700 (37)	354 (29)	410 (27)	40 (25)	166 (26)	149 (29)
C (3)	356 (22)	300 (24)	309 (22)	27 (18)	11 (18)	45 (19)
C (4)	415 (32)	715 (45)	557 (36)	−99 (33)	1 (26)	−145 (32)
C (5)	499 (39)	1366 (85)	601 (42)	−193 (53)	82 (33)	−337 (49)
C (6)	450 (39)	1926 (128)	420 (39)	170 (54)	7 (30)	−103 (59)
C (7)	555 (46)	1717 (109)	315 (32)	165 (55)	47 (31)	517 (68)
C (8)	496 (31)	880 (51)	284 (24)	109 (30)	117 (23)	249 (36)
C (9)	395 (23)	526 (31)	323 (22)	16 (29)	42 (18)	47 (29)
O (10)	1015 (35)	267 (21)	736 (30)	−84 (21)	184 (26)	8 (24)
S (1′)	375 (6)	315 (6)	275 (5)	−65 (6)	44 (4)	−18 (6)
C (3′)	379 (24)	372 (26)	302 (20)	10 (25)	95 (18)	15 (26)
C (4′)	505 (27)	381 (30)	296 (22)	−37 (19)	−26 (20)	83 (22)
C (5′)	379 (23)	448 (33)	400 (25)	−106 (26)	−18 (19)	20 (27)
Cl (6′)	576 (9)	916 (14)	455 (8)	7 (8)	227 (7)	201 (9)
O (7′)	677 (26)	1043 (40)	358 (20)	−200 (25)	−20 (19)	31 (29)
C (8′)	736 (48)	721 (51)	591 (42)	−60 (37)	−135 (37)	341 (41)
C (9′)	581 (41)	894 (62)	673 (47)	−224 (44)	18 (36)	−346 (42)
O (10′)	548 (23)	370 (21)	621 (24)	−291 (19)	−45 (18)	21 (18)

The structure analysis establishes the synthetic product to be 4, 2-oxoindoline-3-spiro-2′-(3′-chloro-5′,5′-dimethyl-4′-oxothiolane-1′-oxide).



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The atomic distances and angles are given with standard deviations in Table 4. No correction was made for thermal motion. The average bond distance and angle in the benzene ring are 1·384 Å and 120·0° respectively. The individual values do not

TABLE 3. FRACTIONAL ATOMIC COORDINATES WITH THEIR STANDARD DEVIATIONS ($\times 10^3$) AND ISOTROPIC TEMPERATURE FACTORS WITH STANDARD DEVIATIONS FOR THE HYDROGEN ATOMS. THE FIRST APPENDED NUMBER REFERS TO THAT OF THE PARENT ATOM

	x $\sigma(x)$	y $\sigma(y)$	z $\sigma(z)$	B σ(B)Å^2
H (11)	−0·139 (10)	0·524 (9)	0·077 (11)	7·5 (2·1)
H (41)	−0·118 (10)	0·063 (8)	0·229 (10)	6·3 (2·0)
H (51)	−0·358 (11)	0·011 (8)	0·036 (11)	7·6 (2.1)
H (61)	−0·502 (9)	0·167 (8)	−0·119 (9)	6·1 (1·7)
H (71)	−0·384 (10)	0·385 (8)	−0·077 (10)	5·7 (1·9)
H (31′)	−0·005 (8)	0·164 (7)	0·508 (10)	5·7 (1·4)
H (81′)	0·493 (12)	0·130 (10)	0·342 (13)	10·1 (2·7)
H (82′)	0·309 (10)	0·076 (8)	0·456 (10)	6·2 (1·9)
H (83′)	0·473 (8)	0·147 (7)	0·578 (10)	5·4 (1·6)
H (91′)	0·530 (11)	0·328 (10)	0·315 (12)	9·3 (2·4)
H (92′)	0·491 (9)	0·382 (6)	0·535 (11)	5·9 (1·8)
H (93′)	0·371 (10)	0·436 (8)	0·363 (10)	6·6 (2·1)

differ significantly from the averages. In the five membered ring of the indole nucleus the two CN bond lengths of 1·41 Å and 1·36 Å (adjacent to the keto group) are similar to those in *e.g.* gliotoxin[6] and diketopiperazine.[7] The two CS bonds of 1·90 Å and 1·86 Å are somewhat longer than previously reported for sulphoxides[8] whereas the SO distance is as expected (1·48 Å). Long CS bonds have been reported earlier in compounds containing a disulphide group.[6] In the strained four membered ring of 1-thiacyclobutane-3-carboxylic acid-1-oxide[9] the CS distances are 1·85 Å and 1·83 Å. The SO bond is in this case 1·53 Å.

The least-squares refinement also gave satisfactory results for all hydrogen parameters. The CH bonds range from 0·90 Å to 1·11 Å with an average value of 1·03 Å.

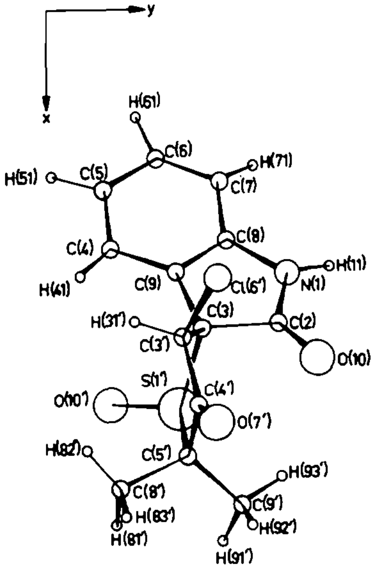

FIG. 1. Spacial drawing of $C_{13}H_{12}ClNO_3S$ with the atomic numbering indicated.

TABLE 4. BOND LENGTHS AND ANGLES AND THEIR ESTIMATED STANDARD DEVIATIONS

Bond lengths (Å)		$\sigma \times 10^3$Å	Bond angles (°)		$\sigma \times 10$
N(1)-C(2)	1·357	(8)	C(2)-N(1)-C(8)	112·9	(6)
N(1)-C(8)	1·410	(10)	N(1)-C(2)-C(3)	105·2	(5)
C(2)-C(3)	1·544	(8)	N(1)-C(2)-O(10)	129·7	(6)
C(2)-O(10)	1·194	(8)	C(3)-C(2)-O(10)	125·0	(5)
C(3)-C(9)	1·481	(7)	C(2)-C(3)-C(9)	104·6	(4)
C(3)-S(1′)	1·897	(5)	C(5)-C(4)-C(9)	116·4	(7)
C(3)-C(3′)	1·520	(6)	C(4)-C(5)-C(6)	122·2	(11)
C(4)-C(5)	1·398	(10)	C(5)-C(6)-C(7)	121·4	(8)
C(4)-C(9)	1·393	(10)	C(6)-C(7)-C(8)	117·5	(11)
C(5)-C(6)	1·356	(17)	C(7)-C(8)-C(9)	121·4	(9)
C(6)-C(7)	1·392	(23)	N(1)-C(8)-C(7)	129·4	(9)
C(7)-C(8)	1·374	(10)	N(1)-C(8)-C(9)	109·1	(5)
C(8)-C(9)	1·389	(9)	C(3)-C(9)-C(8)	107·9	(6)
S(1′)-C(5′)	1·863	(5)	C(3)-C(9)-C(4)	130·9	(5)
S(1′)-O(10′)	1·480	(4)	C(4)-C(9)-C(8)	121·1	(5)
C(3′)-C(4′)	1·501	(7)	C(3)-S(1′)-C(5′)	92·9	(2)
C(3′)-Cl(6′)	1·744	(5)	C(3)-S(1′)-O(10)′	106·8	(2)
C(4′)-C(5′)	1·539	(7)	C(5′)-S(1′)-O(10′)	108·1	(2)
C(4′)-O(7′)	1·195	(6)	S(1′)-C(3)-C(3′)	105·1	(3)
C(5′)-C(8′)	1·523	(10)	S(1′)-C(3)-C(9)	111·3	(3)
C(5′)-C(9′)	1·509	(11)	S(1′)-C(3)-C(2)	103·7	(3)
N(1)-H(11)	0·98	(9)	C(2)-C(3)-C(3′)	112·8	(4)
C(4)-H(41)	0·97	(8)	C(9)-C(3)-C(3′)	118·4	(4)
C(5)-H(51)	1·06	(9)	C(3)-C(3′)-C(4′)	109·2	(4)
C(6)-H(61)	1·04	(7)	C(3)-C(3′)-Cl(6′)	113·1	(4)
C(7)-H(71)	0·90	(8)	C(4′)-C(3′)-Cl(6′)	112·7	(4)
C(8′)-H(81′)	1·11	(10)	C(3′)-C(4′)-C(5′)	112·0	(4)
C(8′)-H(82′)	1·06	(9)	C(3′)-C(4′)-O(7′)	126·0	(5)
C(8′)-H(83′)	1·05	(7)	C(5′)-C(4′)-O(7′)	122·0	(5)
C(9′)-H(91′)	1·11	(9)	S(1′)-C(5′)-C(4′)	107·4	(3)
C(9′)-H(92′)	1·02	(8)	S(1′)-C(5′)-C(8′)	108·2	(4)
C(9′)-H(93′)	1·02	(9)	S(1′)-C(5′)-C(9′)	109·2	(4)
			C(4′)-C(5′)-C(8′)	109·1	(5)
			C(4′)-C(5′)-C(9′)	110·3	(5)
			C(8′)-C(5′)-C(9′)	112·6	(5)

The NH bond is 0·98 Å. The average value for all angles involving hydrogens is 120° in the benzene ring and 109° for the Me groups.

The indole nucleus is not quite planar. The best least-squares plane through the benzene ring is $-0{\cdot}63238X + 0{\cdot}16346Y + 0{\cdot}75722Z - 0{\cdot}25288 = 0$. C(9) shows a maximum deviation from the plane of 0·014 Å. C(2) deviates 0·13 Å from the plane and O(10) as much as 0·23 Å. The angle between the planes formed by the benzene ring and the five membered ring is 2·9°. A similar bending (2·1°) of the indole nucleus has also been observed in 5-methoxy-(N, N)-dimethyltryptamine hydrochloride.[10]

Four of the atoms of the sulphur containing ring are planar within 0·04 Å whereas the fifth atom (C(3′)) is 0·52 Å out of the plane. This plane is roughly perpendicular (96°) to that of the five membered ring of the indole nucleus.

The molecular packing is illustrated by a stereo drawing in Fig. 2, and in Fig. 3 where some intra- and intermolecular contacts are shown. The molecules are held together by hydrogen bonds almost parallel with the *b* axis between N(1) and O(10'). The NO distance is 2·78 Å and the N-H - - O angle is 150°.

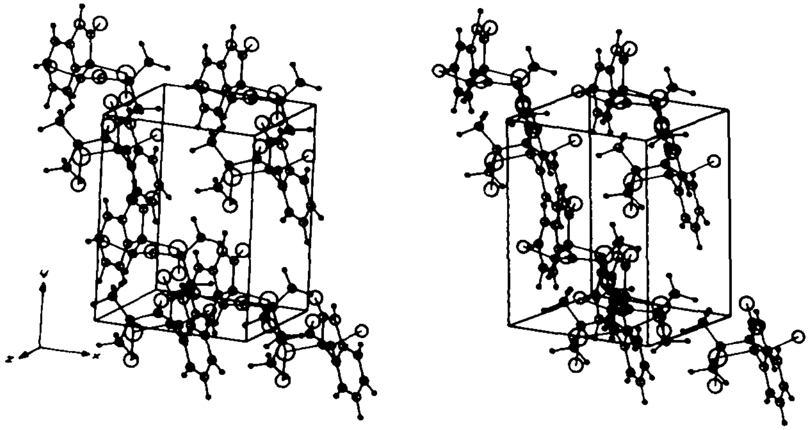

FIG. 2. Stereoscopic pair of $C_{13}H_{12}ClNO_3S$.

There is a short intermolecular contact of 2·23 Å between O(10) and H(31'). This leads to an opening of the angle N(1) C(2) O(10) to 129·7°. The counteracting intramolecular closest contact of O(10) is 2·48 Å to H(93') of one Me group. The Me groups are in intermolecular packing contacts both with each other and with the benzene ring. In the latter case the shortest HH distance is 2·21 Å between H(83')

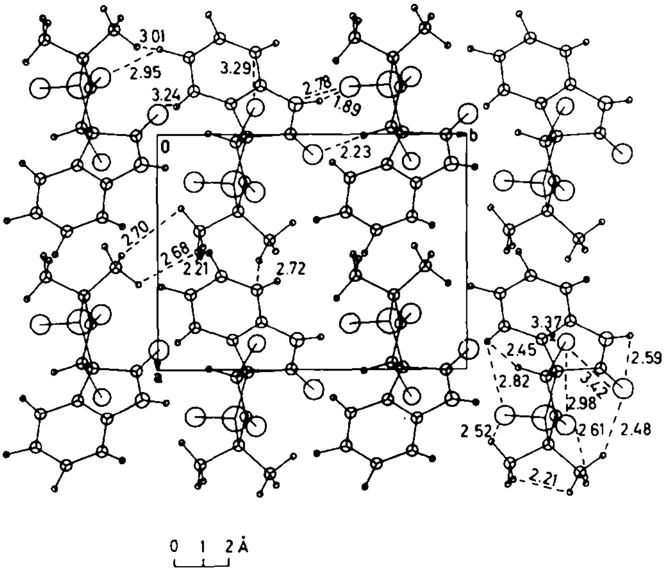

FIG. 3. Molecular packing of $C_{13}H_{12}ClNO_3S$. Some short intra- and intermolecular contacts are shown. The molecules are seen along the *c* axis as in Fig. 1.

and H(61). The planes of the three hydrogen atoms of the Me groups are in contact (around 2·70 Å) with the triangular bases rotated approximately 60° relative to each other. The closest intermolecular contact of the chlorine atom is 3·29 Å to C(7). The intramolecular distance to O(7′) is quite short (2·98 Å) which again results in a large C(3′) C(4′) O(7′) angle (126°). The chlorine atom cannot itself bend away due to other intramolecular contacts.

EXPERIMENTAL

2-Oxoindoline-3-spiro-2′-(3′-chloro-5′,5′-dimethyl-4′-oxothiolane-1′-oxide. Method A. 3-(3-Methyl-2-oxobutyl)-3-hydroxyoxindole[1] (23·3 g, 0·1 mole) was added in ten portions during 0·5 hr to $SOCl_2$ (180 ml) at 20° under stirring. Every addition caused vigorous evolution of SO_2 and HCl. About 20 min after the tenth addition a solid separated from the, at the time, clear, light brown solution. The solid was collected after another 4 hr, washed with light petroleum (40–60°) and dried. Crude yield: 19 g. The solid was crystallized three times from EtOH to give **4** as colourless crystals (8·1 g, 28%) m.p. 190–200° (decomp. with red-colouration). (Calc. for $C_{13}H_{12}ClNO_3S$: C, 52·2; H, 4·1; Cl, 11·9; N, 4·3; O, 16·1. Found: C, 52·3; H, 4·4; Cl, 11·8; N, 4·6; O, 16·3%). MS: 299 (3), 297 (6), (M^+); 251 (2), 249 (6); 215 (11), 214 (6), 213 (12); 186 (5), 185 (9), 184 (8); 181 (34), 180 (17), 179 (100); 172 (20); and below *m/e* 172 the following strong (>15%) peaks: 144 (52), 116 (51), 90 (95), 89 (36). It is suggested that the main fragment, which may be ionized 3-(chloromethylene)-oxindole, is formed from the mother ion *via* elimination of SO and dimethyl ketene. NMR(DMSO-d_6): (τ) 8·52 (s, 3H, Me); 8·35 (s, 3H, Me); 3·51 (s, 1H, CH); 1·2 (s, 1H, NH).

Method B. 3-(3-Methyl-2-oxobutylidene) oxindole[11] (**3**) was used as starting material instead of **1** (R = OH, n = 0), Yield: 35%.

Crystal data

Unit cell monoclinic $a = 8{\cdot}324$ (4), $b = 10{\cdot}982$ (6), $c = 7{\cdot}271$ (3)Å. $\beta = 93{\cdot}12$ (5)° Absent spectra $0k0$ for k odd: Spacegroup $P2_1$: $V = 663{\cdot}7$ Å^3: Molecular weight 297·8: $D_c = 1{\cdot}490$ g cm^{-3}: $Z = 2$: $\lambda = 1{\cdot}54051$ Å ($CuK\alpha_1$ radiation).

A single crystal with dimensions 0·14 · 0·12 · 0·07 mm^3 was mounted along the a-axis and data were collected on a Picker four circle automatic diffractometer using graphite monochromatized CuKα radiation.

The $\theta/2\theta$ scanning mode was used to measure the reflections at a scanning rate of 1 degree min^{-1} and with 10 sec. background counts at each side.

Reflections were measured up to a maximum of 120° in 2θ. 1114 nonsymmetry-related reflections were obtained of which 128 were less than 4σ and considered as unobserved.

$\sigma = (I + (BG \times T/BGT))^{\frac{1}{2}}$ where I = measured intensity: BG = background count: T = time for measured reflection, BGT = time for background measurement.

The data were corrected for the Lorentz and polarization factors but not for absorption or extinction.

Acknowledgements—Grants in support of the Crystallography Group have been obtained from the Swedish Medical, the Swedish Natural Science and the Swedish Technical Research Councils. Grants have also been obtained from the Tricentennial Fund of the Bank of Sweden and the US Public Health Service (GM 11653).

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