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Quinones and Related Compounds in Higher Plants. XIII.[1] Absolute Structure of 2-Carboxy-2-prenyl-4-oxo-1-tetralone, a Key Intermediate in the Biosynthesis of Naphthoquinone Congeners of *Catalpa ovata*

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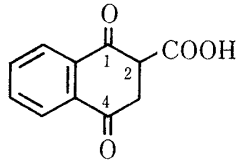
The absolute configuration at C-2 of 2-carboxy-2-prenyl-4-oxo-1-tetralone (**2**), a key intermediate in the biosynthesis of prenylnaphthoquinone congeners of the wood and callus tissues of *Catalpa ovata*, was verified to be *S* by X-ray crystallographic analysis of the *p*-bromobenzoate (**8**) derived from **2**.

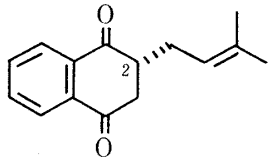
Keywords——(2*S*)-(−)-2-carboxy-2-prenyl-4-oxo-1-tetralone; biosynthetic intermediate; prenylnaphthoquinones; absolute structure; X-ray analysis

In the course of studies on the naphthoquinone congeners of the wood and tissue cultures of *Catalpa ovata* G. DON (Bignoniaceae), we clarified their biosynthetic pathway.[2–6] In particular, by radiochemical dilution experiments, we demonstrated that the stereochemical course in the biosynthesis of (2*R*)-(−)-catalponone ((2*R*)-**1**) from 2-carboxy-4-oxo-1-tetralone

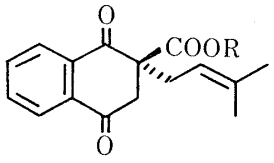
(COT) proceeds *via* (2*S*)-(—)-2-prenyl-2-carboxy-4-oxo-1-tetralone ((2*S*)-**2**) through stereoselective prenylation and successive decarboxylation with retention of the configuration. The absolute configurations of both enantiomers of prenyl-COT methyl ester (**3**) used for this experiment were inferred on the basis of the circular dichroism spectra of *p*-bromobenzoates of their reduction products (**4**) on C-1. In view of the key intermediary role of prenyl-COT



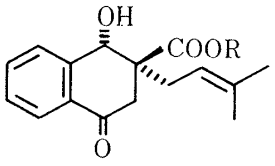
COT



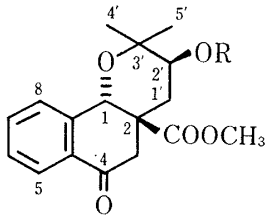
(2*R*)-(−)-**1**

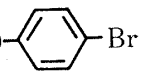


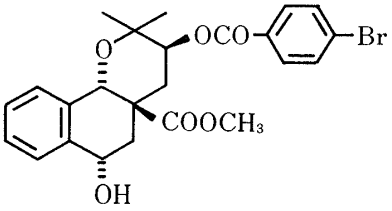
(2*S*)-**2** : R=H
(2*S*)-(−)-**3** : R=CH_3



(1*S*, 2*S*)-(+)-**4** : R=CH_3
(1*S*, 2*S*)-(+)-**5** : R=H



(1*S*, 2*S*, 2′*S*)-(−)-**6**: R=H
(1*S*, 2*S*, 2′*S*)-(−)-**7**: R=CO- 



(1*S*, 2*S*, 4*R*, 2′*S*)-(+)-**8**

Fig. 1

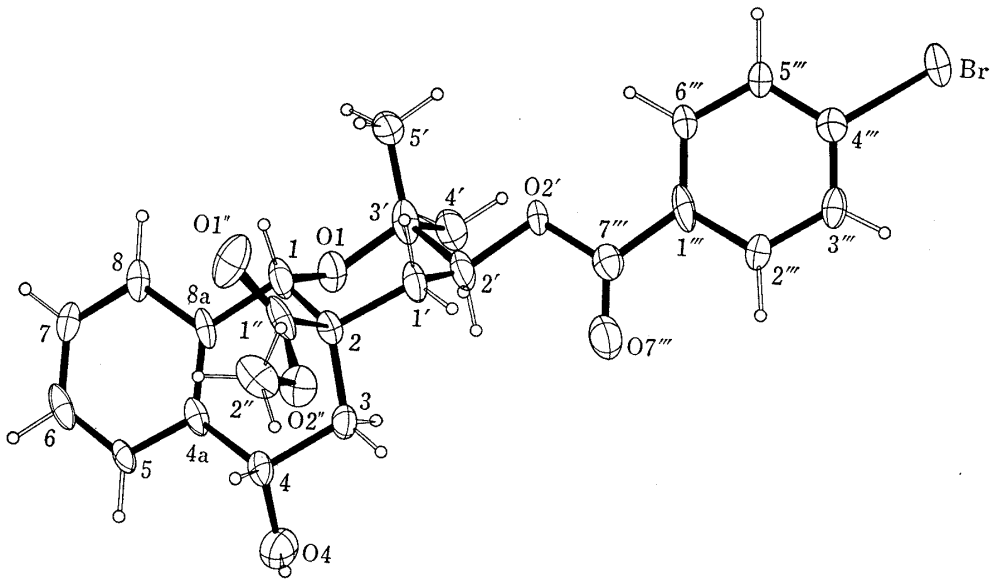


Fig. 2

(**2**) in the biosynthesis of prenylnaphthoquinones, however, it seemed desirable to confirm the absolute structures of both enantiomers of **3**. This paper deals with the verification of the presumed absolute structures of both enantiomers of prenyl-COT methyl ester (**3**) by the X-ray crystallographic analysis of a derivative of one enantiomer of **3**.

The crystalline derivative suitable for this purpose was obtained in the following way: dextrorotatory acid ((+)-**5**) obtained through the resolution of racemic 2-carboxy-2-prenyl-4-oxo-1-tetralol (**5**) was methylated with diazomethane to the methyl ester ((+)-**4**), which gave the tricyclic compound (**6**) on treatment with *m*-chloroperbenzoic acid and *p*-toluenesulfonic acid, in the same way as for the racemate (**4**).[6] The spectral properties of this compound coincided with those of the corresponding racemate. Compound (−)-**6** was then converted through treatment with *p*-bromobenzoyl chloride into the *p*-bromobenzoate ((−)-**7**).

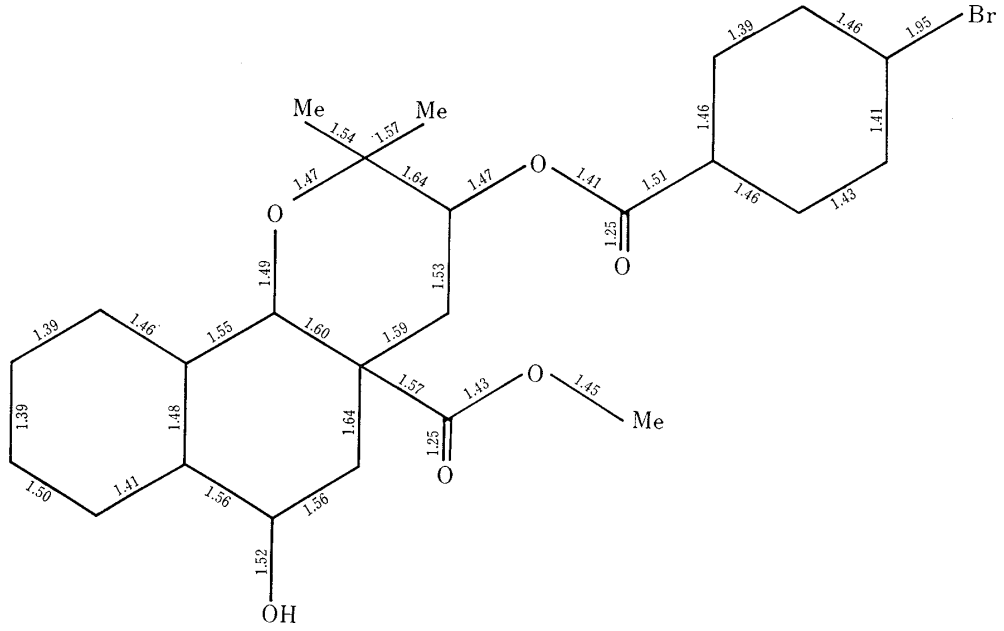


Fig. 3

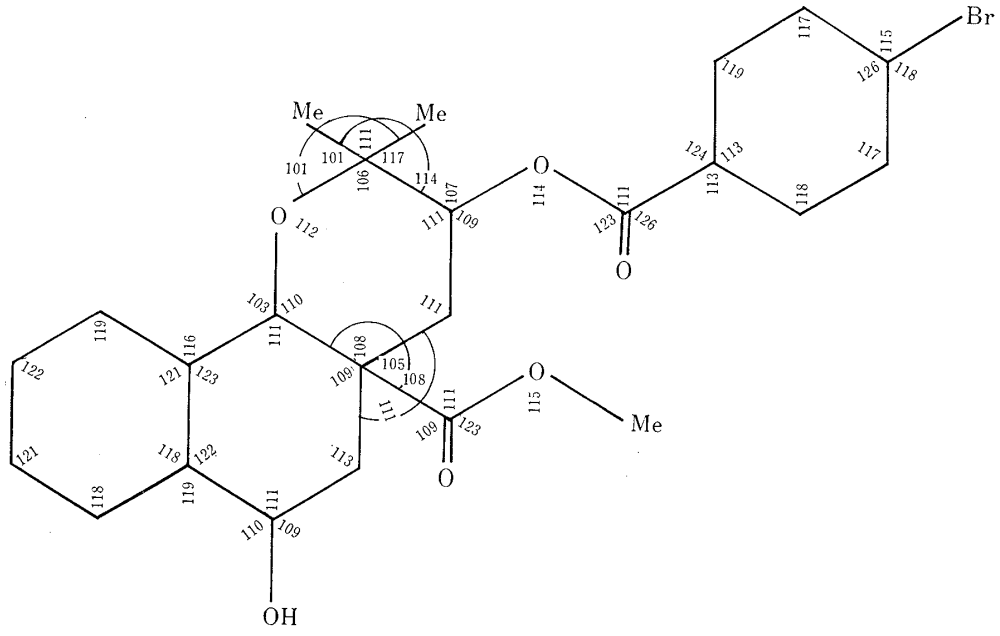


Fig. 4

Finally, on reduction with sodium borohydride the latter gave colorless plates of (+)-**8**, mp 234—236°, $[\alpha]_D^{26}$ +71.3°, which was subjected to the X-ray diffraction analysis.

A stereoscopic view of the structure of this compound determined by the X-ray analysis is shown in Fig. 2. The absolute structure was determined on the basis of the anomalous scattering of the bromine atom. The bond lengths and angles calculated from the atomic parameters in Table I (*vide post*) are given in Fig. 3 and Fig. 4, respectively.

These results indicated the (1*S*, 2*S*, 4*R*, 2′*S*)-configuration for (+)-**8**. Accordingly, it was confirmed that (−)-prenyl-COT methyl ester (**3**), and therefore, the corresponding acid, have the (*S*)-configuration at C-2 as presumed from the CD spectral study of the *p*-bromobenzoate of (+)-**4**.

Experimental

For general directions, see Part 9[7] in this series unless otherwise stated. Intensity data were measured on a Rigaku AFC5 diffractometer using the ω-2θ scanning technique.

Preparation of *p*-Bromobenzoate (7)——The optically active compound ((−)-**6**) was prepared in the manner reported for the preparation of (±)-**6**.[6] *p*-Bromobenzoyl chloride (86 mg) was added to a solution of (−)-**6** (63 mg) in pyridine (0.85 ml) and the solution was left overnight at room temperature. The mixture was diluted with ice-water and extracted with $CHCl_3$. The $CHCl_3$ layer was washed successively with satd. $NaHCO_3$ and H_2O, and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave a residue (120 mg), which was subjected to PLC (C_6H_6–EtOAc 6 : 4). A crystalline residue (45 mg) obtained from the eluate of a band at around *Rf* 0.66 was recrystallized from $CHCl_3$ to give (−)-**7** (34 mg) as prisms, mp 239—241°. $[\alpha]_D^{26}$ −4.59°

Table I. Atomic Parameters and Their Estimated Standard Deviations

	X	*Y*	*Z*	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br	−1536(1)	0(0)	−1306(2)	55(0)	361(0)	137(0)	−4(0)	−27(0)	−6(0)
C(1)	7071(13)	856(29)	2773(17)	50(11)	279(60)	127(20)	−5(20)	−26(12)	−49(27)
C(2)	6357(12)	−471(20)	3335(14)	67(11)	49(30)	110(16)	−26(15)	−18(11)	27(18)
C(3)	6064(11)	89(34)	4591(13)	54(9)	194(40)	107(16)	12(29)	1(9)	−19(36)
C(4)	7132(12)	283(27)	5399(15)	59(10)	130(41)	129(18)	47(22)	−11(10)	−31(27)
C(4a)	8078(12)	1173(25)	4820(15)	47(11)	171(40)	110(18)	27(18)	−21(11)	−4(23)
C(5)	9003(13)	1752(25)	5482(15)	62(12)	182(44)	107(18)	56(20)	−23(11)	11(25)
C(6)	9888(19)	2635(30)	4913(24)	59(14)	117(36)	144(20)	39(18)	−47(13)	2(23)
C(7)	9880(15)	2703(32)	3752(19)	63(14)	282(64)	163(26)	−9(25)	20(15)	−7(35)
C(8)	8992(12)	2126(26)	3066(16)	46(11)	164(41)	126(19)	16(19)	−2(11)	−11(27)
C(8a)	8053(11)	1409(24)	3589(15)	39(10)	145(39)	129(18)	27(17)	−32(11)	−10(24)
C(1′)	5254(13)	−752(25)	2554(16)	59(12)	183(49)	116(19)	12(19)	−15(12)	−32(23)
C(2′)	4630(12)	775(26)	2323(15)	50(11)	222(52)	110(17)	−10(18)	−29(11)	−56(23)
C(3′)	5439(14)	2064(29)	1773(19)	67(13)	169(46)	189(26)	−11(23)	−28(15)	−19(34)
C(4′)	4835(18)	3642(34)	1827(20)	106(19)	288(63)	144(25)	−13(31)	−18(17)	18(35)
C(5′)	5786(15)	1726(31)	550(16)	82(15)	317(61)	92(18)	27(28)	−7(13)	−24(30)
C(1″)	7026(14)	−2036(25)	3301(17)	77(13)	116(39)	142(21)	−16(19)	−64(13)	−18(24)
C(2″)	7246(19)	−4593(29)	4156(19)	164(23)	94(44)	155(23)	30(28)	−30(18)	7(26)
C(1‴)	1739(11)	−105(32)	1085(16)	48(10)	140(38)	174(21)	50(22)	−30(11)	−67(34)
C(2‴)	696(12)	−580(18)	1546(15)	54(10)	42(27)	124(18)	23(14)	11(11)	0(18)
C(3‴)	−292(12)	−594(23)	812(16)	46(10)	146(43)	146(20)	45(17)	8(11)	−3(24)
C(4‴)	−185(11)	−134(30)	−312(12)	62(10)	109(32)	93(14)	6(25)	−3(9)	−10(28)
C(5‴)	840(12)	395(32)	−789(15)	58(11)	278(60)	100(17)	−2(25)	2(10)	−5(29)
C(6‴)	1808(11)	385(28)	−75(14)	55(10)	177(48)	112(17)	10(21)	−13(10)	−2(25)
C(7‴)	2702(13)	−23(36)	1964(14)	83(13)	155(40)	122(17)	38(31)	−6(11)	−15(35)
O(1)	6389(9)	2292(19)	2604(11)	70(9)	181(28)	122(13)	7(15)	−6(8)	15(18)
O(4)	6820(11)	1177(22)	6436(13)	109(13)	309(39)	146(16)	−52(19)	31(11)	−29(22)
O(2′)	3688(7)	506(17)	1500(10)	42(7)	207(33)	119(12)	8(13)	−19(7)	−6(16)
O(1″)	7757(12)	−2350(19)	2631(15)	108(13)	181(32)	240(23)	39(18)	73(14)	47(24)
O(2″)	6736(11)	−3064(17)	4179(12)	112(12)	116(27)	160(16)	34(16)	4(11)	38(19)
O(7‴)	2667(9)	−434(22)	2983(11)	74(9)	309(45)	146(14)	2(19)	−14(9)	53(23)

Positional parameters are multiplied by 10^4. Anisotropic temperature factors are multiplied by 10^3. Anisotropic temperature factors are in the form $T=\exp\{-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hk+2\beta_{23}kl)\}$.

(c, 1.31, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1715, 1690, 1590, 850. ^1H NMR ($CDCl_3$) δ: 1.30 and 1.65 (each s, $-O\rangle C\langle^{CH_3}_{CH_3}$), 2.18 (dd, $J=13.5$ and 6.0 Hz, 1′-H_{eq}), 2.47 (dd, $J=13.5$ and 10.0 Hz, 1′-H_{ax}), 2.95 (dd, $J=17.0$ and 1.0 Hz, 3-H_{eq}), 3.14 (d, $J=17.0$ Hz, 3-H_{ax}), 3.52 (s, $COOCH_3$), 5.14 (br s, 1-H), 5.22 (dd, $J=10.0$ and 6.0 Hz, 2′-H) and 7.20—8.17 (m, 8×aromatic H). *Anal.* Calcd for $C_{24}H_{23}BrO_6$: C, 59.15; H, 4.76; Br, 16.40. Found: C, 59.11; H, 4.86; Br, 16.67.

Reduction of the *p*-Bromobenzoate (7) with $NaBH_4$——$NaBH_4$ (13 mg) was added to a solution of (−)-**7** (41 mg) in dioxane (5 ml) containing two drops of H_2O and the mixture was stirred for 24 hr at room temperature. The reaction solution was diluted with H_2O, acidified to pH 3 with 1 N HCl and extracted with $CHCl_3$. The extract was washed successively with satd. $NaHCO_3$ and H_2O and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave a residue which was subjected to PLC (ether). A crystalline residue (39 mg) obtained from the eluate of a band at around *Rf* 0.60 was recrystallized from ether to give (+)-**8** as colorless plates, mp 234—236°. $[\alpha]_D^{25}$ +71.3° (c, 0.645, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3530, 1705, 1600, 865. ^1H NMR ($CDCl_3$) δ: 1.27 and 1.52 (each s, $-O\rangle C\langle^{CH_3}_{CH_3}$), 2.25 and 2.30 (each d, $J=7.5$ Hz, 3-H_2), 3.53 (s, $COOCH_3$), 4.68 (dd, $J=10.0$ and 6.0 Hz, 2′-H), 5.01 (s, 1-H), 5.18 (t, $J=7.5$ Hz, 4-H), 7.07—8.20 (m, 8×aromatic H). *Anal.* Calcd for $C_{24}H_{25}BrO_6$: C, 58.91; H, 5.15. Found: C, 58.61; H, 4.97.

Crystal Data for *p*-Bromobenzoate (8)——The crystal of (+)-**8** was monoclinic, space group $P2_1$, with two molecules in a unit cell of dimensions $a=11.97$ (5) Å, $b=8.59$ (6) Å, $c=11.94$ (12) Å and $\beta=93.7$ (7), $V=1225.4$ Å^3, $D_{calc}=1.340$ g/cm^3. The intensities of 1297 reflections were observed ($F_o/\sigma(F_o)>3.0$).

Table II. Positional Parameters of Hydrogen Atoms

	X	Y	Z
H(1)	7360	278	2090
H(3A)	5642	1172	4548
H(3B)	5553	−645	4948
H(4)	7496	−676	5590
H(5)	9010	1533	6292
H(6)	10500	3200	5430
H(7)	10492	3223	3375
H(8)	9000	2367	2188
H(1′A)	4739	−1540	2865
H(1′B)	5463	−1139	1774
H(2′)	4392	1200	3114
H(4′A)	4612	3785	2606
H(4′B)	5390	4477	1647
H(4′C)	4177	3691	1282
H(5′A)	6171	674	516
H(5′B)	5148	1755	−14
H(5′C)	6359	2540	350
H(2″A)	6992	−5304	4808
H(2″B)	7028	−5208	3446
H(2″C)	8082	−4562	4250
H(2‴)	586	−902	2377
H(3‴)	−1000	−902	1050
H(5‴)	921	902	−1669
H(6‴)	2565	902	−397
H(O4)	6729	9	6729

The values are multiplied by 10^4.

Determination of the Absolute Structure of the (+)-*p*-Bromobenzoate ((+)-8)——The structure of compound (+)-**8** was solved by the heavy-atom method. The position of the bromine atom was obtained from the Harker section at $v=0.5$ on the Patterson map. The positions of all the non-hydrogen atoms were observed in the first Fourier map based on the bromine atom position. The structure was refined by the block-diagonal least-squares method. Several cycles of least-squares refinement with anisotropic thermal parameters reduced the R-value to 0.080. Hydrogen atoms with isotropic temperature factors (3.0 Å^2), whose positions were obtained from the difference Fourier map, were included in the structure factor calculation at the last cycle. The absolute configuration was determined on the basis of the anomalous dispersion term in the atomic scattering factor of the bromine atom. For thirty-two Bijvoet reflections having large discrepancies in the observed paired intensities, the differences of the observed structure amplitudes were

Table III. Structure Amplitudes of Bijvoet Pairs

n	k	l	F_o	F_c	n	k	l	F_o	F_c
4	1	0	39.0	35.9	4	$\bar{1}$	0	41.2	35.9
9	1	0	18.1	16.5	9	$\bar{1}$	0	20.3	18.0
11	1	0	2.7	1.5	11	$\bar{1}$	0	4.9	3.7
1	2	0	32.7	25.7	1	$\bar{2}$	0	36.3	28.1
4	2	0	42.3	39.9	4	$\bar{2}$	0	37.9	35.5
10	2	0	25.8	22.3	10	$\bar{2}$	0	27.7	24.1
11	2	0	8.2	7.7	11	$\bar{2}$	0	9.6	9.2
1	3	0	26.5	23.5	1	$\bar{3}$	0	24.2	20.0
2	3	0	21.9	17.8	2	$\bar{3}$	0	19.9	15.2
3	3	0	66.7	54.6	3	$\bar{3}$	0	69.1	56.1
4	3	0	20.3	11.7	4	$\bar{3}$	0	24.3	14.6
6	3	0	8.7	8.9	6	$\bar{3}$	0	5.8	6.6
8	3	0	37.7	32.3	8	$\bar{3}$	0	35.1	30.7
0	4	0	80.7	66.4	0	$\bar{4}$	0	83.8	67.4
3	4	0	1.7	3.1	3	$\bar{4}$	0	8.3	3.8
9	4	0	18.1	14.0	9	$\bar{4}$	0	15.9	13.1
10	4	0	16.2	13.2	10	$\bar{4}$	0	17.5	14.8
12	4	0	24.3	7.4	12	$\bar{4}$	0	10.2	7.9
2	5	0	21.3	15.2	2	$\bar{5}$	0	23.3	16.4
1	5	0	18.9	11.6	1	$\bar{5}$	0	23.5	13.9
4	5	0	19.9	16.4	4	$\bar{5}$	0	22.8	17.8
6	5	0	10.4	12.2	6	$\bar{5}$	0	7.5	11.0
8	5	0	10.7	10.1	8	$\bar{5}$	0	6.7	8.3
10	5	0	3.1	2.2	10	$\bar{5}$	0	0.0	1.7
12	5	0	14.1	7.0	12	$\bar{5}$	0	6.8	6.3
13	5	0	2.4	1.6	13	$\bar{5}$	0	6.5	1.5
0	6	0	8.7	10.7	0	$\bar{6}$	0	7.1	10.7
5	6	0	12.8	10.4	5	$\bar{6}$	0	8.2	10.6
6	6	0	10.0	7.4	6	$\bar{6}$	0	8.0	8.7
7	6	0	8.9	11.6	7	$\bar{6}$	0	10.7	11.7
11	6	0	2.6	3.3	11	$\bar{6}$	0	7.0	3.7
12	6	0	9.1	4.7	12	$\bar{6}$	0	5.7	4.7

compared with those of the structure amplitudes calculated for the two enantiomorphic structures, and the final atomic parameters with their standard deviations for the correct structure are listed in Tables I and II. The observed structure amplitudes of the selected Bijvoet reflections and those calculated by the use of the correct parameters given in Tables I and II are listed in Table III.

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