La principale différence entre les deux molécules intervient au niveau de la jonction *B/C*. L'aplatissement général de la molécule (Fig. 2) se traduit par une légère variation des angles de torsions, notamment des angles C(11)–C(8)–C(9)–C(14) et C(10)–C(8)–C(9)–C(7). L'atome d'oxygène O(3) occupe le site traditionnel déterminé pour les stéroïdes oestrogènes (Précigoux, 1978).

Le groupe hydroxyméthyle situé sur la position $17\beta$ occupe deux positions statistiques. L'une des positions de l'atome d'oxygène, O(598) sur la Fig. 2, est la même que celle trouvée pour la molécule d'hydroxyméthyle-$17\beta$ oestratriène-1,3,5(10) ol-3 déjà citée, mais l'autre, O(98), est différente. Un calcul théorique utilisant le programme *GEMO* (Delettré, 1978) a mis en évidence la possibilité de trois positions pour ce groupement dont deux d'entre elles correspondent aux deux positions trouvées dans le cristal.

Les distances intramoléculaires existant entre l'atome O(3) et les atomes O(98) et O(598) sont respectivement égales à 11,3 et 12,3 Å. La cohésion cristalline est assurée par des liaisons de van der Waals et un réseau de liaisons hydrogène statistiques suivant l'occupation des sites O(98) et O(598). La Fig. 3 rend compte des trois possibilités statistiques.

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# Structure of *N*-(*tert*-Butoxycarbonyl)-L-prolyl-L-valylglycine Hemihydrate

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**Abstract.** $C_{17}H_{29}N_3O_6.\frac{1}{2}H_2O$, $M_r = 380{\cdot}44$, $P2_1$, $a = 15{\cdot}783\,(2)$, $b = 13{\cdot}428\,(2)$, $c = 9{\cdot}815\,(2)$ Å, $\beta = 90{\cdot}94\,(1)^\circ$, $D_o = 1{\cdot}19$, $D_c$ $(Z = 4) = 1{\cdot}21$ Mg m$^{-3}$, m.p. 444–445 K; there are two independent molecules in an asymmetric unit. The structure was solved by the vector-space search method, and the final $R$ index was 0·084. The crystal packing, in which two molecules are dimerized *via* $\beta$-sheet-type hydrogen bonds, is similar to that of the previously reported Boc-Pro-Ile-Gly-OH.

**Introduction.** Structures of some sequentially related oligopeptides have been studied in our laboratory to elucidate relationships between an amino acid sequence and its conformation, which is one of the central themes of the structural chemistry of peptides and proteins. In these studies the Boc-Pro-*X*-Gly-OH group is of considerable interest because of its conformational variety, *i.e.* the $\beta$-turn structure of Boc-Pro-Leu-Gly-OH (Ashida, Tanaka, Shimonishi & Kakudo, 1977), the polyproline II type and the $\beta$-turn structure of Boc-Pro-Pro-Gly-$NH_2$ (Tanaka, Ashida, Shimonishi & Kakudo, 1979), and the dimer structure formed *via* $\beta$-sheet-type hydrogen bonds in Boc-Pro-Ile-Gly-OH (Yamada, Tanaka & Ashida, 1980). Following the study of these peptides, the structure of Boc-Pro-Val-Gly-OH is described in this paper.

The peptide was synthesized step-wise using dicyclohexylcarbodiimide as a condensation reagent with the protecting groups of *tert*-butoxycarbonyl and benzyl ester. The C-terminal benzyl group was finally removed and the product was crystallized from an ethyl acetate solution.

A crystal of dimensions 0·15 × 0·15 × 0·3 mm was used for the X-ray experiment. Intensity measurements were made on a Rigaku four-circle diffractometer with Ni-filtered Cu $K\alpha$ radiation up to $2\theta = 120^\circ$. 3233 independent reflections were collected, of which 375 were considered to be non-observed. Lp corrections were made but no absorption correction was applied.

The crystal has two crystallographically independent peptide molecules and one water molecule in an

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asymmetric unit. After several unsuccessful attempts by the direct method, the vector-space search method was applied on the assumption that the molecule has either a *β*-turn or an extended conformation. For the *β*-turn model, 16 atoms of Boc-Pro-Leu-Gly-OH (Ashida *et al.*, 1977) were used, while for the extended model 20 atoms of Boc-Pro-Ile-Gly-OH (Yamada *et al.*, 1980) were used. The translational search, preceded by the rotational one, with the extended model produced two prominent peaks, which were later shown to correspond to the two independent molecules. The

Table 1. *Atomic parameters* ($\times 10^4$, $B_{eq} \times 10$) *with e.s.d.'s in parentheses for the nonhydrogen atoms*

| | $x$ | $y$ | $z$ | $B_{\text{eq}}$ (Å$^2$) |
|---|---|---|---|---|
| O(1)*A* | 588 (3) | 6000 (4) | −1394 (4) | 58 (2) |
| O(2)*A* | −818 (3) | 6163 (5) | −1912 (5) | 75 (3) |
| O(3)*A* | 416 (3) | 3905 (4) | 578 (6) | 64 (3) |
| O(4)*A* | 2694 (3) | 4223 (4) | 3895 (5) | 66 (3) |
| O(5)*A* | 3588 (3) | 2112 (5) | 4667 (6) | 70 (3) |
| O(6)*A* | 3521 (6) | 2563 (9) | 6781 (7) | 145 (6) |
| N(1)*A* | −353 (3) | 5739 (5) | 195 (5) | 51 (3) |
| N(2)*A* | 1504 (3) | 4563 (4) | 1763 (5) | 46 (2) |
| N(3)*A* | 2012 (4) | 2776 (5) | 4099 (8) | 72 (4) |
| C(1)*A* | 624 (8) | 7381 (11) | −2975 (12) | 117 (8) |
| C(2)*A* | 1840 (5) | 6283 (11) | −2544 (9) | 104 (7) |
| C(3)*A* | 613 (7) | 5670 (13) | −3815 (10) | 127 (8) |
| C(4)*A* | 894 (5) | 6346 (7) | −2717 (7) | 67 (4) |
| C(5)*A* | −226 (4) | 5986 (6) | −1111 (7) | 54 (3) |
| C(6)*A* | 323 (4) | 5634 (5) | 1226 (6) | 47 (3) |
| C(7)*A* | −171 (4) | 5724 (8) | 2552 (7) | 66 (4) |
| C(8)*A* | −1034 (5) | 5439 (12) | 2205 (9) | 109 (7) |
| C(9)*A* | −1215 (4) | 5680 (7) | 768 (7) | 61 (4) |
| C(10)*A* | 753 (4) | 4622 (5) | 1125 (6) | 47 (3) |
| C(11)*A* | 1948 (4) | 3616 (5) | 1904 (7) | 49 (3) |
| C(12)*A* | 2725 (5) | 3515 (6) | 963 (8) | 63 (4) |
| C(13)*A* | 3131 (5) | 2521 (7) | 1116 (10) | 77 (5) |
| C(14)*A* | 2407 (7) | 3687 (8) | −523 (10) | 88 (6) |
| C(15)*A* | 2263 (4) | 3565 (5) | 3382 (7) | 53 (3) |
| C(16)*A* | 2269 (5) | 2671 (9) | 5513 (10) | 96 (6) |
| C(17)*A* | 3204 (6) | 2436 (8) | 5717 (10) | 85 (5) |
| O(1)*B* | 4412 (2) | −437 (4) | 6363 (8) | 51 (2) |
| O(2)*B* | 3324 (3) | −484 (4) | 4826 (5) | 61 (2) |
| O(3)*B* | 5208 (3) | 1786 (4) | 5058 (5) | 56 (2) |
| O(4)*B* | 8063 (3) | 1440 (4) | 6833 (5) | 54 (2) |
| O(5)*B* | 9794 (3) | 3539 (5) | 8180 (6) | 77 (3) |
| O(6)*B* | 8476 (3) | 3422 (6) | 8940 (6) | 87 (3) |
| N(1)*B* | 4647 (3) | −86 (4) | 4217 (5) | 48 (2) |
| N(2)*B* | 6371 (3) | 1103 (4) | 6073 (5) | 42 (2) |
| N(3)*B* | 7860 (3) | 3048 (4) | 6357 (6) | 51 (3) |
| C(1)*B* | 4637 (6) | −879 (9) | 8626 (9) | 89 (6) |
| C(2)*B* | 3353 (7) | 40 (11) | 7915 (13) | 112 (7) |
| C(3)*B* | 3524 (8) | −1754 (8) | 7262 (11) | 104 (7) |
| C(4)*B* | 3945 (4) | −783 (6) | 7542 (8) | 57 (4) |
| C(5)*B* | 4074 (4) | −351 (5) | 5117 (6) | 46 (3) |
| C(6)*B* | 5554 (4) | 63 (6) | 4524 (7) | 53 (3) |
| C(7)*B* | 5930 (6) | 147 (9) | 3093 (9) | 88 (5) |
| C(8)*B* | 5185 (8) | 454 (11) | 2201 (10) | 127 (9) |
| C(9)*B* | 4405 (6) | 78 (7) | 2769 (8) | 70 (4) |
| C(10)*B* | 5669 (4) | 1058 (5) | 5254 (6) | 47 (3) |
| C(11)*B* | 6637 (4) | 2044 (5) | 6699 (6) | 44 (3) |
| C(12)*B* | 6353 (5) | 2160 (6) | 8202 (7) | 57 (3) |
| C(13)*B* | 5385 (5) | 2176 (7) | 8291 (8) | 72 (4) |
| C(14)*B* | 6743 (5) | 1394 (7) | 9144 (8) | 72 (5) |
| C(15)*B* | 7585 (4) | 2135 (5) | 6616 (6) | 44 (3) |
| C(16)*B* | 8749 (4) | 3299 (6) | 6553 (7) | 58 (4) |
| C(17)*B* | 8982 (4) | 3432 (6) | 8029 (8) | 60 (4) |
| O(*W*) | 1784 (5) | 621 (7) | 4157 (9) | 115 (5) |

Table 2. *Hydrogen positional parameters* ($\times 10^3$) *with their e.s.d.'s in parentheses*

| | $x$ | $y$ | $z$ | Bonded to |
|---|---|---|---|---|
| H(1) | 168 (4) | 520 (5) | 210 (7) | N(2)*A* |
| H(2) | 673 (4) | 45 (5) | 615 (7) | N(2)*B* |
| H(3) | 161 (4) | 227 (6) | 357 (7) | N(3)*A* |
| H(4) | 749 (4) | 356 (6) | 613 (7) | N(3)*B* |
| H(5) | 77 (4) | 755 (5) | −398 (7) | C(1)*A* |
| H(6) | 84 (4) | 779 (5) | −216 (7) | C(1)*A* |
| H(7) | −3 (4) | 746 (5) | −303 (7) | C(1)*A* |
| H(8) | 439 (4) | −105 (5) | 947 (7) | C(1)*B* |
| H(9) | 489 (4) | −21 (5) | 874 (7) | C(1)*B* |
| H(10) | 505 (4) | −152 (6) | 830 (7) | C(1)*B* |
| H(11) | 217 (4) | 643 (5) | −331 (7) | C(2)*A* |
| H(12) | 197 (4) | 553 (5) | −229 (7) | C(2)*A* |
| H(13) | 202 (4) | 654 (5) | −165 (7) | C(2)*A* |
| H(14) | 298 (4) | −22 (6) | 873 (7) | C(2)*B* |
| H(15) | 278 (4) | 9 (6) | 712 (7) | C(2)*B* |
| H(16) | 359 (4) | 63 (6) | 800 (7) | C(2)*B* |
| H(17) | 88 (4) | 588 (6) | −464 (7) | C(3)*A* |
| H(18) | 7 (4) | 545 (5) | −381 (7) | C(3)*A* |
| H(19) | 79 (4) | 501 (6) | −353 (7) | C(3)*A* |
| H(20) | 330 (4) | −209 (6) | 810 (7) | C(3)*B* |
| H(21) | 396 (4) | −223 (5) | 691 (7) | C(3)*B* |
| H(22) | 305 (4) | −173 (6) | 652 (7) | C(3)*B* |
| H(23) | 78 (4) | 616 (5) | 111 (7) | C(6)*A* |
| H(24) | 585 (4) | −49 (6) | 509 (7) | C(6)*B* |
| H(25) | −23 (4) | 652 (6) | 287 (7) | C(7)*A* |
| H(26) | 12 (4) | 532 (5) | 336 (7) | C(7)*A* |
| H(27) | 619 (4) | −53 (6) | 281 (7) | C(7)*B* |
| H(28) | 644 (4) | 63 (6) | 302 (7) | C(7)*B* |
| H(29) | −148 (4) | 556 (6) | 296 (7) | C(8)*A* |
| H(30) | −103 (4) | 462 (6) | 236 (7) | C(8)*A* |
| H(31) | 526 (4) | 33 (5) | 116 (7) | C(8)*B* |
| H(32) | 522 (4) | 126 (5) | 215 (7) | C(8)*B* |
| H(33) | −150 (4) | 635 (5) | 64 (7) | C(9)*A* |
| H(34) | −155 (4) | 512 (5) | 22 (7) | C(9)*A* |
| H(35) | 432 (4) | −60 (6) | 233 (7) | C(9)*B* |
| H(36) | 389 (4) | 55 (5) | 275 (7) | C(9)*B* |
| H(37) | 155 (4) | 298 (6) | 167 (7) | C(11)*A* |
| H(38) | 630 (4) | 256 (5) | 620 (7) | C(11)*B* |
| H(39) | 318 (4) | 408 (6) | 129 (7) | C(12)*A* |
| H(40) | 663 (4) | 288 (6) | 856 (7) | C(12)*B* |
| H(41) | 358 (4) | 244 (5) | 34 (7) | C(13)*A* |
| H(42) | 268 (4) | 200 (6) | 97 (7) | C(13)*A* |
| H(43) | 336 (4) | 229 (5) | 209 (7) | C(13)*A* |
| H(44) | 519 (4) | 227 (5) | 933 (6) | C(13)*B* |
| H(45) | 512 (4) | 153 (6) | 797 (7) | C(13)*B* |
| H(46) | 518 (4) | 272 (5) | 767 (7) | C(13)*B* |
| H(47) | 297 (4) | 357 (5) | −114 (7) | C(14)*A* |
| H(48) | 221 (4) | 441 (6) | −62 (7) | C(14)*A* |
| H(49) | 198 (4) | 315 (6) | −81 (7) | C(14)*A* |
| H(50) | 651 (4) | 163 (6) | 1017 (7) | C(14)*B* |
| H(51) | 738 (4) | 149 (5) | 911 (7) | C(14)*B* |
| H(52) | 648 (4) | 67 (6) | 880 (7) | C(14)*B* |
| H(53) | 194 (4) | 217 (6) | 604 (7) | C(16)*A* |
| H(54) | 221 (4) | 340 (6) | 601 (7) | C(16)*A* |
| H(55) | 887 (4) | 395 (5) | 599 (7) | C(16)*B* |
| H(56) | 912 (4) | 260 (5) | 611 (7) | C(16)*B* |
| H(57) | 414 (4) | 202 (6) | 481 (7) | O(5)*A* |
| H(58) | 1001 (4) | 359 (6) | 906 (7) | O(5)*B* |
| H(59) | 235 (4) | 20 (5) | 440 (7) | O(*W*) |
| H(60) | 140 (4) | 83 (6) | 328 (7) | O(*W*) |

whole structure was solved by the partial-structure tangent refinement method (Karle, 1968) based on one of the two molecular fragments thus obtained.

The structure was refined by the least-squares method with the program *HBLS* V (Ashida, 1973). The function minimized was $\sum w(|F_o| - |F_c|)^2$, where weights $w$ were unity for all the non-zero reflections and zero for zero reflections. The final $R$ value including all the H atoms was 0·084 for all the reflections and 0·064 for non-zero reflections. The final positional parameters are listed in Tables 1 and 2.* All atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). The isotropic temperature factor $B = 5{\cdot}141$ Å$^2$ was assigned to all the H atoms.

**Discussion.** The crystal structure projected along the $c$ axis is shown in Fig. 1. The bond lengths, angles and torsion angles are given in Fig. 2. The overall shapes of the two independent molecules are not very different and possess a very similar conformation to the extended one of Boc-Pro-Ile-Gly-OH (Yamada *et al.*, 1980). A more precise comparison of the torsion angles and the least-squares discrepancy between corresponding atoms showed that the conformational similarity between molecule $A$ of Boc-Pro-Val-Gly-OH and Boc-Pro-Ile-Gly-OH is higher than that between molecules $A$ and $B$ of Boc-Pro-Val-Gly-OH. This seems to suggest that conformational fluctuation to this extent (18·4° is the maximum deviation with respect to the torsion angles) is not caused directly by the difference of the side chains but mainly by the crystal-packing requirements.

The conformational similarity is closely related to that of the molecular interactions in the crystal; *i.e.* Boc-Pro-Val-Gly-OH peptides dimerize *via* two NH···O hydrogen bonds in a similar way as in the Boc-Pro-Ile-Gly-OH crystal although the former does not possess an exact twofold rotation axis within the dimer. The abundant van der Waals contacts within the dimer suggest a plausible crystallization process which

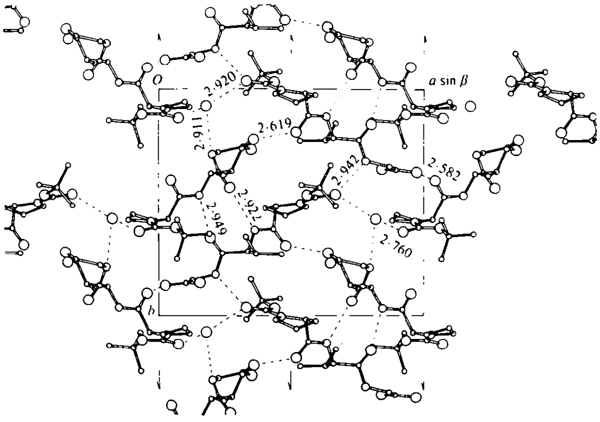
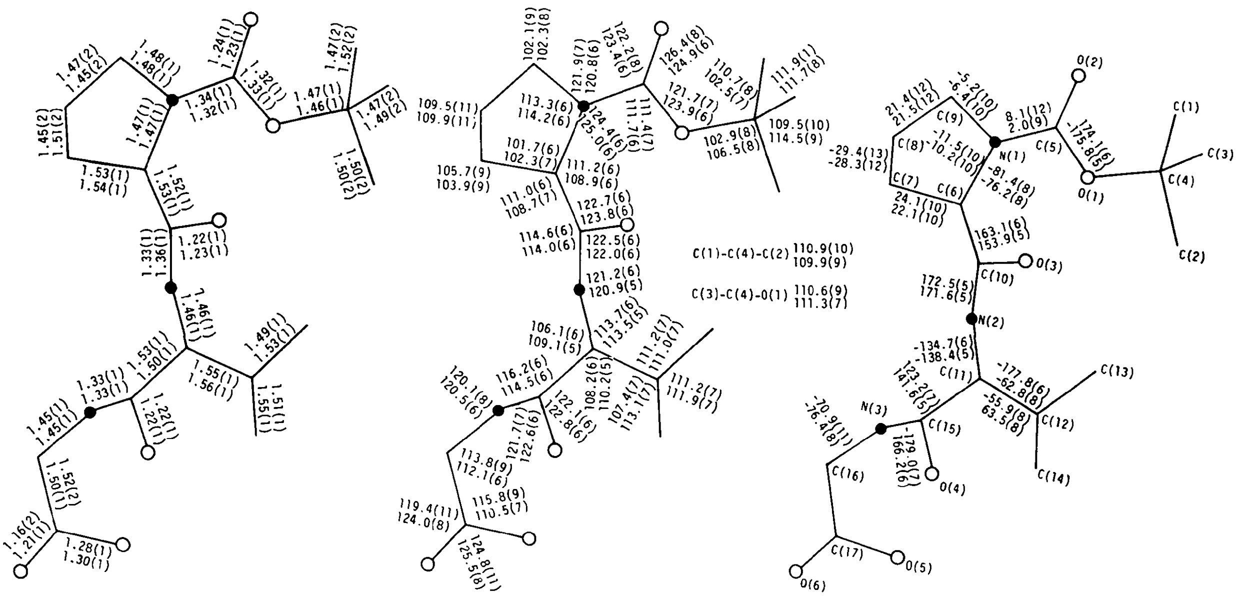


Fig. 1. The crystal structure viewed along the $c$ axis. The hydrogen bonds are shown by broken lines. The standard deviations for the hydrogen-bond distances are 0·007–0·012 Å.



(*a*) (*b*) (*c*)

Fig. 2. (*a*) Bond lengths (Å), (*b*) bond angles (°), and (*c*) torsion angles (°) for molecules $A$ (upper) and $B$ (lower).

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35234 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

involves dimerization at an early stage. The hydrogen-bonding pattern in the dimer is that of the well known antiparallel $\beta$-sheet structure, as shown in Fig. 3. In the present case, however, the two molecules are not exactly in a plane perpendicular to the twofold axis in order to avoid interaction between the Boc and COOH groups. This kind of dimerization by the $\beta$-sheet hydrogen bonds related by a twofold or quasi-twofold axis sometimes occurs in peptide crystals, *e.g.* Z-Gly-Pro-OH (Tanaka, Kojima, Ashida, Tanaka & Kakudo, 1977) and Z-Gly-D,L-Pro-OH (Kojima, Yamane & Ashida, 1978). A structural comparison of these dimers will be reported elsewhere (Ashida & Tanaka, 1980).

The water molecule in the present crystal at a general position acts not only as a hydrogen donor but also as a hydrogen acceptor. This is one of the main differences from the Boc-Pro-Ile-Gly-OH crystal (Yamada *et al.*, 1980) in which the water molecule on the twofold axis with about half occupancy acts only as a hydrogen donor. This suggests that a water molecule acting as a hydrogen acceptor is important for stoichiometric cocrystallization. The two peptide molecules *A* and *B* in this crystal differ mainly in their hydrogen-bonding schemes with the water molecules, as shown in Table 3.

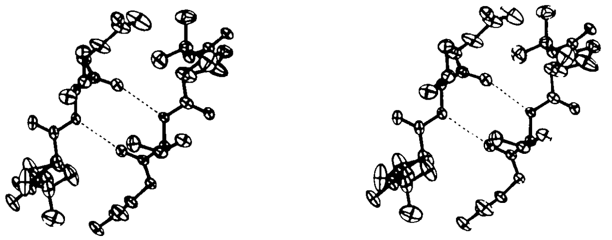

Fig. 3. Stereodrawing of the dimer structures formed *via* the $\beta$-sheet-type hydrogen bonds.

Table 3. *Hydrogen bonds*

| Donor | Acceptor | |
|---|---|---|
| O(5)$A$ | O(3)$B$ | 2·619 (8) Å |
| O(5)$B$ | O(3)$A^{\rm i}$ | 2·582 (9) |
| N(2)$A$ | O(4)$B^{\rm ii}$ | 2·949 (7) |
| N(2)$B$ | O(4)$A^{\rm iii}$ | 2·922 (7) |
| N(3)$A$ | O($W$) | 2·911 (12) |
| N(3)$B$ | O(2)$B^{\rm ii}$ | 2·942 (8) |
| O($W$) | O(2)$B$ | 2·920 (10) |
| O($W$) | O(2)$A^{\rm iv}$ | 2·760 (11) |

| Symmetry code | |
|---|---|
| (i) | $1·0 + x, y, 1·0 + z$ |
| (ii) | $1·0 - x, 0·5 + y, 1·0 - z$ |
| (iii) | $1·0 - x, -0·5 + y, 1·0 - z$ |
| (iv) | $-x, -0·5 + y, -z$ |

It may be worthwhile comparing the side-chain conformations in valine (Torii & Iitaka, 1970), isoleucine (Torii & Iitaka, 1971) and Boc-Pro-Val-Gly-OH. All of these crystals contain two different molecules with different side-chain conformations. The valyl side chains of the present molecules are *trans* for *A* and *gauche* II for *B*, while they are *trans* and *gauche* I for both valine and isoleucine. This phenomenon may reflect the fact that these different side-chain conformations are almost equally stable.

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