# X-Ray Crystal Structure of L-Tryptophan–Picric Acid Charge-Transfer Complex and Comparison with DL-Tryptophan–Picric Acid Complex[1)]

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**In order to investigate the difference between the indole–picric acid interaction modes formed in the L- and DL-tryptophan–picric acid complex crystals, the crystal structure of the former complex was analysed by the X-ray diffraction method and the interaction geometry observed was compared with that of the latter complex crystal already analysed. Two crystallographically independent charge-transfer interaction pairs were formed in the crystal structure and formed discrete stacking layers consisting of tryptophan and picric acid molecules. The indole and picric acid planes were parallely stacked with an interplanar spacing near to 3.4 Å in both pairs. This reflects the structural feature necessary for the charge-transfer interaction characterized by the red coloration of complex crystal. Three kinds of indole–picric acid stacking geometries observed were similar with one another, and one of them was almost the same as that in the DL-tryptophan–picric acid complex crystal. This indicates that the observed indole–picric acid interaction mode reflects an intrinsic feature and is not significantly affected by the different chirality of the tryptophan side chain and crystal environment.**

**Keywords** L-tryptophan–picric acid complex; charge-transfer complex; crystal structure; stacking interaction; molecular conformation

## Introduction

Indole compounds exist widely in living cells and function in various biologically important roles, primarily as tryptophan residues in proteins and as indolealkylamines such as serotonin and tryptamine. Indole compounds are known to form the charge-transfer complexes with a variety of aromatic acceptors[2)] because of the excellent $\pi$-electron donating ability of the indole ring,[3)] and their complex structures with pyridine, flavin and thiamin coenzymes[4)] and with nucleic acid bases[5)] have been analysed by the X-ray diffraction method.

On the other hand, concerning the charge-transfer complexes in which tryptophan participates, the crystallographic studies are rather few,[6)] although they have been implicated as important in such a biological process as the binding model of substrate or coenzyme to the tryptophan residue in enzyme. Therefore, the present paper deals with the crystal structure of L-tryptophan picric acid (1 : 1) complex as an interaction model of L-tryptophan with a typical aromatic acceptor. Since the crystal structure of DL-tryptophan–picric acid complex was already analysed by Gartland *et al.*,[7)] the present study makes it possible to determine to what extent the racemization of tryptophan (and thus the different crystal packing) affects the interaction mode between the tryptophan and picric acid molecules.

## Experimental

**Preparation of Complex Crystals** Single crystals of L-tryptophan–picric acid complex were obtained as reddish needles upon mixing an aqueous solution of equimolar L-tryptophan and picric acid and by slowly evaporating the solution at room temperature (20 °C). The red coloring of these crystals is indicative of the charge-transfer complex because of the different color from its component colorless tryptophan and yellow picric acid.

**Crystal Data Collection** A single crystal with the dimension of $0.1 \times 0.1 \times 0.4\,mm^3$ was used for the following X-ray study. Details of crystal data and the reflectional intensity data collection are summarized in Table I. Unit-cell dimensions were determined by a least-squares fit of $2\theta$ angles of 25 reflections ranging of $30° \leq 2\theta \leq 60°$. Crystal density was measured by the flotation method using a $C_6H_6/CCl_4$ mixture. Intensity data were measured by the graphite-monochromated Cu$K_\alpha$ radiation ($\lambda = 1.5418$ Å) on an automated Rigaku AFC-5 diffractometer and were collected by employing a $\omega - 2\theta$ scanning mode where the background was counted for 5 s at both extremes of each peak. Four standard reflections were monitored for every 100 reflection intervals and showed no significant time-dependence ($< \pm 2\%$). The observed intensities were corrected for Lorentz and polarization effects. No corrections for absorption and extinction effects were made.

**Crystal Structure Solution and Refinement** After many attempts, the structure was finally solved by the direct method with the SHELXS86[8)] and TEXSAN programs.[9)] Many non-H atoms were revealed on an E-map calculated by the tangent refinement method using the $E$ values of 1.40—2.50 which were calculated from the observed intensities by the assistance of the atomic coordinates[7)] of DL-tryptophan–picric acid

TABLE I. Summary of Crystal Data and Intensity Collection Details

| | |
|---|---|
| Formula | $C_{11}H_{12}N_2O_2 \cdot C_6H_3N_3O_7$ |
| $M_r$ | 433.334 |
| Crystal system | Orthorhombic |
| Space group | $P2_12_12_1$ |
| $a$, Å | 7.802 (3) |
| $b$, Å | 15.482 (4) |
| $c$, Å | 31.134 (52) |
| $V$, Å$^3$ | 3761 (7) |
| $Z$ | 8 |
| $D_m$, g·cm$^{-3}$ | 1.508 (3) |
| $D_x$, g·cm$^{-3}$ | 1.531 |
| $\mu$(Cu$K_\alpha$), cm$^{-1}$ | 982 |
| $F$(000) | 1792 |
| Temperature of data collection, °C | 20 |
| Scan speed in $2\theta$, °min$^{-1}$ | 4 |
| Scan range in $\omega$, ° | $1.10 + 0.15 \tan\theta$ |
| Data range measured | $-9 \leq h \leq 0$, $0 \leq k \leq 18$, $0 \leq l \leq 36$ |
| No. of unique data measured | 3652 |
| No. of data used for refinement ($M$) | 3093 for $F_o \geq 2\sigma(F_o)$ |
| No. of variables ($N$) | 675 |
| $R$ | 0.074 |
| $Rw$ | 0.078 |
| $S$ (goodness of fit) | 1.6167 |

complex as a random group. The positional parameters of the non-H atoms were refined by full-matrix least-squares with anisotropic thermal parameters. The positions of H atoms were obtained from a difference Fourier map and were included in the subsequent refinements with isotropic thermal parameters. The function minimized was $\sum w(|F_o|-|F_c|)^2$, where $|F_o|$ and $|F_c|$ are the observed and calculated amplitudes of structure factors, respectively. The weighting scheme used for the final refinement was $w=1.0/\sigma(F_o)^2$, where $\sigma(F_o)^2$ is the standard deviation of each reflection intensity on the basis of counting statistics. Final $R$ $(=\sum(|F_o|-|F_c|)/\sum|F_o|)$, $Rw$ $(=[\sum w(|F_o|-|F_c|)^2/\sum w|F_o|^2]^{1/2})$, and $S$ $(=[\sum w(|F_o|-|F_c|)^2/(M-N)]^{1/2})$ are also given in Table I. None of the positional parameters for non-H atoms shifted more than their estimated standard deviations (e.s.d.s). The residual electron density in the final difference Fourier map ranged from $-0.69$ $e\cdot Å^{-3}$ to 0.65 $e\cdot Å^{-3}$. Final positional and isotropic thermal parameters for non-H atoms are listed in Table II,[10] together with their e.s.d.s in parentheses, where two independent interaction pairs between the tryptophan and picric acid molecules are classified as pairs I and II, respectively. For all crystallographic computation, the UNICS program[11] was used, and the atomic scattering factors and terms of anomalous dispersion corrections were taken from ref. 12.

**Quantum Chemical Calculation** Atomic net charges and dipole moments of tryptophan and picric acid molecules were calculated by the MNDO (modified neglect of differential overlap) method by using the atomic co-ordinates in Table II.

All numerical calculations were performed on a Micro VAX II computer at the Computation Center, Osaka University of Pharmaceutical Sciences.

## Results and Discussion

**Molecular Dimensions and Conformation** Stereoscopic views of two crystallographically independent tryptophan and picric acid molecules in pairs I and II (abbreviated as T1, T2, P1 and P2, respectively) are shown in Fig. 1, together with atomic numberings used in this work. The conformational torsion angles are given in Table III. Because of the relatively low ratio of $M/N$ (=3093/675) (Table I), the accuracy for the bond lengths and angles are not so high as usual; the e.s.d.s are in the range of 0.006—0.024 Å for length and 0.4°—1.2° for angle. This would be in part responsible for the zwinning habit of the complex crystal. However, not notable differences were observed between the same bond lengths and angles of two independent molecules, and they are all in the acceptable region, compared with the related data.[13]

Three H atoms tetrahedrally located near the N(12) atom of the T1 molecule, which were clearly observed on a difference Fourier map, and the bond lengths of C(11)–N(12)=1.510(8) Å, C(12)–O(12)=1.283(8) Å and C(12)–O(13)=1.233(8) Å indicate a zwitterionic structure of this molecule with the amino group protonated and carboxyl group deprotonated. A neutral structure of P1 molecule is suggested by the bond length of C(1)–O(1)=1.330(11) Å, though the H atom was not clearly identified on the density map because of the relatively large thermal motion of this molecule. On the other hand, T2 molecule forms a 'salt' with P2 anion, where the amino group of T2 is protonated and the phenol OH of P2 is deprotonated, as judged from the H atom positions found in the electron density map. This is also suggested by their bonding parameters: C(11)–N(12)=1.483(8) Å, C(12)–O(12)=1.307(9) Å, C(12)–O(13)=1.197(8) Å of T2 and C(1)–O(1)=1.258(7) Å of P2.

Molecular conformations of two independent tryptophan are different from each other in such a way that the carboxyl and amino groups are in the *gauche*$^+$ and *trans* positions with respect to the indole ring for T1 and *trans* and *gauche*$^-$ ones for T2. The conformation of the T2 molecule is

TABLE II. Final Atomic Coordinates and Equivalent Values of Anisotropic Temperature Factors with Their e.s.d.s in Parentheses

| Atom | $x$ | $y$ | $z$ | $U_{eq}$ (Å$^2$) |
|---|---|---|---|---|
| Pair I | | | | |
| Tryptophan | | | | |
| N(1) | 0.099 (1) | 0.6239 (5) | 0.2809 (2) | 0.17 (2) |
| C(2) | 0.017 (1) | 0.6463 (5) | 0.3187 (3) | 0.17 (2) |
| C(3) | −0.0327 (9) | 0.5732 (5) | 0.3402 (2) | 0.12 (1) |
| C(4) | 0.008 (1) | 0.4100 (6) | 0.3197 (3) | 0.15 (2) |
| C(5) | 0.070 (1) | 0.3581 (5) | 0.2873 (3) | 0.18 (2) |
| C(6) | 0.149 (1) | 0.3978 (8) | 0.2501 (3) | 0.25 (3) |
| C(7) | 0.163 (1) | 0.4809 (8) | 0.2458 (3) | 0.23 (2) |
| C(8) | 0.097 (1) | 0.5356 (7) | 0.2777 (2) | 0.19 (2) |
| C(9) | 0.0234 (9) | 0.5009 (5) | 0.3142 (2) | 0.13 (1) |
| C(10) | −0.1312 (9) | 0.5710 (5) | 0.3809 (2) | 0.12 (1) |
| C(11) | −0.0221 (8) | 0.5579 (4) | 0.4219 (2) | 0.09 (1) |
| N(12) | −0.1408 (7) | 0.5433 (3) | 0.4595 (2) | 0.080 (9) |
| C(12) | 0.0874 (8) | 0.6337 (4) | 0.4323 (2) | 0.09 (1) |
| O(12) | 0.2286 (6) | 0.6382 (3) | 0.4112 (2) | 0.15 (1) |
| O(13) | 0.0421 (6) | 0.6868 (3) | 0.4596 (1) | 0.094 (8) |
| Picric acid | | | | |
| C(1) | 0.499 (1) | 0.5341 (6) | 0.3223 (3) | 0.17 (2) |
| O(1) | 0.4372 (8) | 0.5960 (5) | 0.3477 (2) | 0.21 (1) |
| C(2) | 0.478 (1) | 0.4446 (6) | 0.3277 (3) | 0.16 (2) |
| N(2) | 0.395 (1) | 0.4107 (5) | 0.3648 (3) | 0.20 (2) |
| O(2) | 0.356 (1) | 0.4600 (5) | 0.3940 (3) | 0.29 (2) |
| O(2′) | 0.376 (1) | 0.3322 (5) | 0.3662 (3) | 0.29 (2) |
| C(3) | 0.540 (1) | 0.3875 (6) | 0.2977 (3) | 0.19 (2) |
| C(4) | 0.623 (1) | 0.4181 (6) | 0.2621 (3) | 0.18 (2) |
| N(4) | 0.694 (1) | 0.3559 (7) | 0.2313 (4) | 0.29 (2) |
| O(4) | 0.703 (1) | 0.2826 (5) | 0.2426 (3) | 0.32 (2) |
| O(4′) | 0.741 (1) | 0.3849 (7) | 0.1973 (3) | 0.43 (3) |
| C(5) | 0.649 (1) | 0.5067 (5) | 0.2548 (3) | 0.17 (2) |
| C(6) | 0.589 (1) | 0.5627 (5) | 0.2850 (3) | 0.14 (2) |
| N(6) | 0.625 (1) | 0.6550 (5) | 0.2767 (2) | 0.18 (2) |
| O(6) | 0.652 (1) | 0.6764 (5) | 0.2403 (3) | 0.35 (2) |
| O(6′) | 0.628 (1) | 0.7055 (5) | 0.3073 (3) | 0.30 (2) |
| Pair II | | | | |
| Tryptophan | | | | |
| N(1) | 0.564 (1) | 0.4864 (6) | 0.6184 (3) | 0.26 (2) |
| C(2) | 0.527 (1) | 0.5625 (7) | 0.6053 (3) | 0.20 (2) |
| C(3) | 0.3571 (8) | 0.5843 (5) | 0.6132 (2) | 0.12 (1) |
| C(4) | 0.121 (1) | 0.4805 (7) | 0.6443 (3) | 0.26 (2) |
| C(5) | 0.104 (2) | 0.3988 (9) | 0.6587 (3) | 0.34 (3) |
| C(6) | 0.239 (3) | 0.3388 (9) | 0.6618 (3) | 0.42 (4) |
| C(7) | 0.392 (2) | 0.3652 (8) | 0.6479 (3) | 0.34 (3) |
| C(8) | 0.419 (1) | 0.4453 (5) | 0.6319 (2) | 0.16 (2) |
| C(9) | 0.2899 (9) | 0.5072 (5) | 0.6299 (2) | 0.12 (2) |
| C(10) | 0.269 (1) | 0.6642 (5) | 0.6064 (2) | 0.15 (2) |
| C(11) | 0.1707 (8) | 0.6699 (4) | 0.5626 (2) | 0.08 (1) |
| N(12) | 0.2950 (7) | 0.6741 (3) | 0.5267 (2) | 0.09 (1) |
| C(12) | 0.0557 (9) | 0.7474 (5) | 0.5611 (2) | 0.11 (1) |
| O(12) | −0.0897 (7) | 0.7323 (3) | 0.5805 (2) | 0.19 (1) |
| O(13) | 0.0970 (6) | 0.8128 (3) | 0.5434 (2) | 0.14 (1) |
| Picric acid | | | | |
| C(1) | 0.1949 (8) | 0.4322 (3) | 0.5225 (2) | 0.06 (1) |
| O(1) | 0.1519 (6) | 0.5036 (3) | 0.5066 (1) | 0.10 (1) |
| C(2) | 0.3639 (8) | 0.3950 (4) | 0.5178 (2) | 0.09 (1) |
| N(2) | 0.4979 (7) | 0.4448 (4) | 0.4977 (2) | 0.11 (1) |
| O(2) | 0.4981 (7) | 0.5217 (3) | 0.4997 (2) | 0.17 (1) |
| O(2′) | 0.6149 (7) | 0.4056 (3) | 0.4805 (2) | 0.22 (1) |
| C(3) | 0.4101 (8) | 0.3145 (5) | 0.5317 (2) | 0.11 (1) |
| C(4) | 0.2925 (8) | 0.2667 (4) | 0.5534 (2) | 0.10 (1) |
| N(4) | 0.3413 (7) | 0.1839 (4) | 0.5706 (2) | 0.13 (1) |
| O(4) | 0.4728 (7) | 0.1481 (3) | 0.5574 (2) | 0.20 (1) |
| O(4′) | 0.2497 (7) | 0.1461 (4) | 0.5967 (2) | 0.18 (1) |
| C(5) | 0.1251 (8) | 0.2945 (4) | 0.5620 (2) | 0.08 (1) |
| C(6) | 0.0839 (8) | 0.3757 (4) | 0.5467 (2) | 0.09 (1) |
| N(6) | −0.0891 (7) | 0.4026 (4) | 0.5577 (2) | 0.14 (1) |
| O(6) | −0.1874 (7) | 0.3527 (4) | 0.5734 (3) | 0.28 (2) |
| O(6′) | −0.1291 (7) | 0.4788 (4) | 0.5530 (2) | 0.21 (1) |

$U_{eq}=1/3\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\boldsymbol{a}_i\boldsymbol{a}_j$.

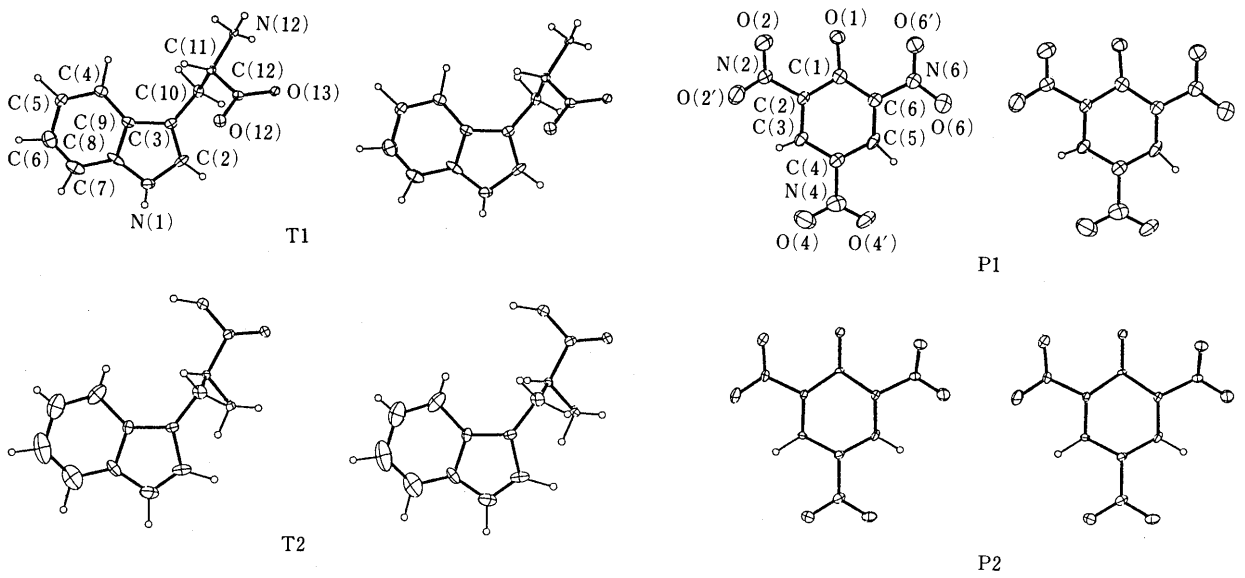


Fig. 1. Stereoscopic Views of Two Crystallographically Independent L-Tryptophan (T1 and T2) and Picric Acid (P1 and P2) Molecules, Together with Atomic Numberings Used in This Paper

Two independent interaction pairs of both molecules are formed by T1 and P1 (pair I) and T2 and P2 (pair II) molecules, respectively.

TABLE III. Conformational Torsion Angles of Two Independent Tryptophan (T1 and T2) and Picric Acid (P1 and P2) Molecules with Their e.s.d.s in Parentheses

| Tryptophan | T1 | T2 |
|---|---|---|
| C(2)–C(3)–C(10)–C(11): $\chi$ | −98.6 (7) | 95.3 (8) |
| C(9)–C(3)–C(10)–C(11) | 84.5 (7) | −84.8 (7) |
| C(3)–C(10)–C(11)–N(12): $\phi$ | −171.4 (6) | −69.4 (5) |
| C(3)–C(10)–C(11)–C(12) | 69.2 (6) | 169.3 (6) |
| C(10)–C(11)–C(12)–O(12) | −81.6 (6) | −82.1 (6) |
| C(10)–C(11)–C(12)–O(13) | 99.0 (7) | 98.8 (7) |
| Picric acid | P1 | P2 |
| C(1)–C(2)–N(2)–O(2) | −6.7 (8) | 28.9 (6) |
| C(1)–C(2)–N(2)–O(2') | 177 (1) | −154.4 (7) |
| C(3)–C(4)–N(4)–O(4) | −13.4 (9) | −16.9 (6) |
| C(3)–C(4)–N(4)–O(4') | 168 (1) | 166.9 (7) |
| C(5)–C(6)–N(6)–O(6) | 22.9 (8) | −9.2 (7) |
| C(5)–C(6)–N(6)–O(6') | −155.8 (9) | 166.6 (7) |

frequently observed in other related crystals such as DL-tryptophan picrate[7] ($\chi=99.4°$, $\phi=-61.2°$), DL-tryptophan formate[14] ($\chi=105.1°$, $\phi=-53.7°$) and 5-hydroxy-DL-tryptophan[15] ($\chi=110.7°$, $\phi=-74.7°$). Contrastly, the T1 molecule shows a rather uncommon conformation that has been observed only for DL-tryptophan[16] ($\chi=-106.6°$, $\phi=-168.6°$). The conformational analysis of tryptophan was already investigated by the NMR in solution[17] and the molecular dynamics simulation method.[18] The latter study suggested that both conformations observed in the present crystal are in one of the most energetically stable regions, although the former study showed that they are different from the dominant species in the solution state ($\chi=ca.\ -90°$, $\phi=ca.\ -60°$).

The benzene moieties of picric acid molecules are essentially coplanar. As found for other crystal structures,[7,19] nitro groups are twisted out of the benzene plane ranging from 7.1°—28.1° around the C–N bond, and such a notable tilting appears to be a conformational feature of picric acid.

**Crystal Structure and Hydrogen Bonds** A stereoscopic view of crystal structure is shown in Fig. 2. Two kinds of molecular packing modes are observed in the crystal structure. One is the packing consisting of pair I, where each molecule is alternately piled up along the *a*-direction, thus forming an infinite stacking layer of ···T1–P1–T1–P1···. The other is the stacking formation of pair II, where two pairs related by a diad screw symmetry form a stacking layer consisting of T2–P2–P2–T2 perpendicular to the *a*-direction. These independent layers, as a whole, are alternately arranged perpendicular to the *c*-direction.

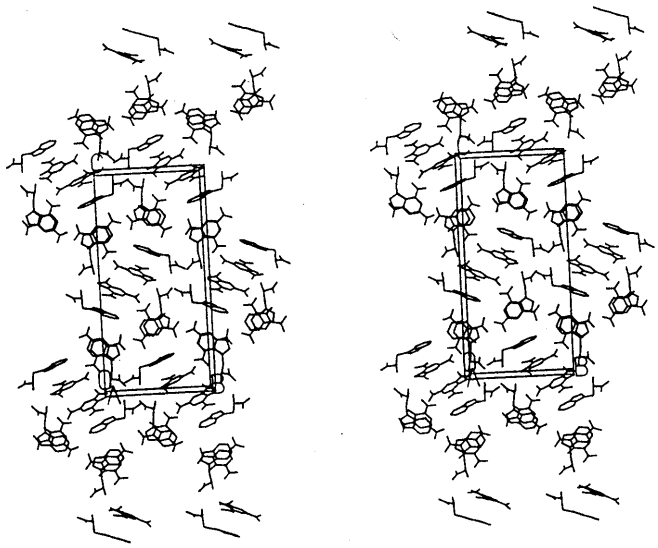

Fig. 2. A Stereoscopic View of Molecular Packings in Crystal Structure, Viewed along the *a*-Direction

The hydrogen bonding network formed in the crystal structure is schematically depicted in Fig. 3, and these hydrogen bonding data, together with the electrostatic interactions, are summarized in Table IV. Pairs I and II are mainly linked to each other by hydrogen bonds in which the tryptophan amino groups participate. The $NH_3^+$ group of T1 forms six hydrogen bonds or electrostatic interactions

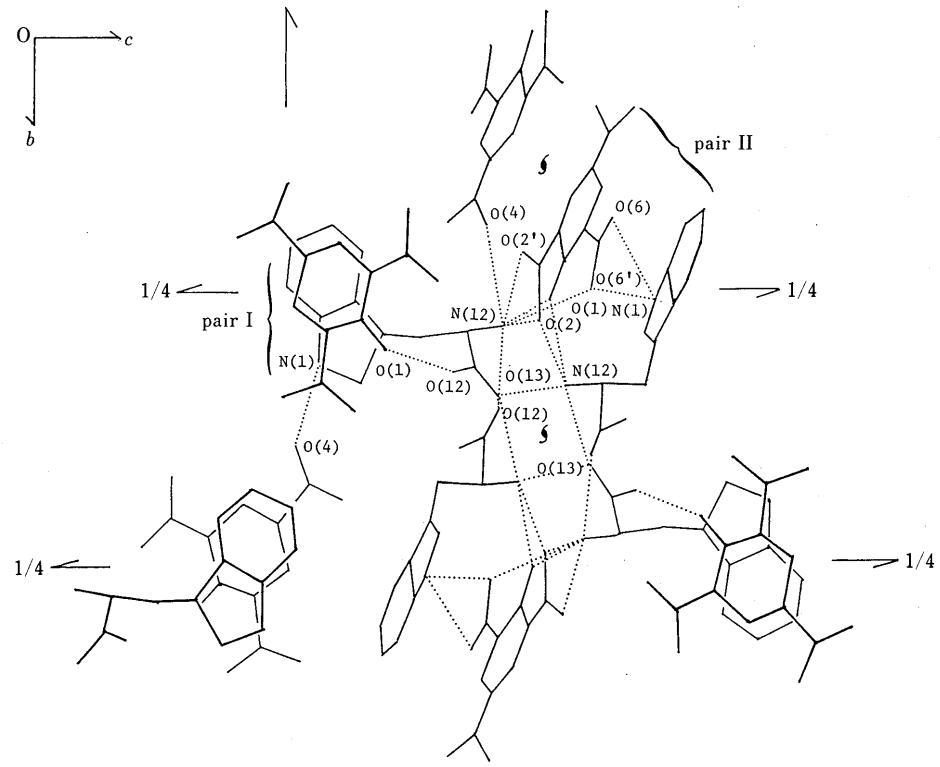


Fig. 3. Schematic Hydrogen-Bonding and Electrostatic Interaction Network Formed in Complex Crystal

The dotted lines represent possible hydrogen bonds.

TABLE IV. Hydrogen Bond Distances and Angles and Electrostatic Interactions[a)]

| Donor (D) at $x, y, z$ | Acceptor (A) at symmetry operation | | Distance (Å) D···A | Distance (Å) H···A | Angle (°) <D–H···A |
|---|---|---|---|---|---|
| N(1)T1 | O(4)P1 | $1-x, y+1/2, 1/2-z$ | 2.991 (11) | 2.47 (14) | 131 (13) |
| N(12)T1 | O(2)P2 | $x-1, y, z$ | 3.100 ( 7) | — | — |
| N(12)T1 | O(2')P2 | $x-1, y, z$ | 2.934 ( 8) | 2.16 (14) | 134 (11) |
| N(12)T1 | O(4)P2 | $x-1/2, 1/2-y, 1-z$ | 3.137 ( 7) | 2.63 (14) | 112 (10) |
| N(12)T1 | O(13)T2 | $x-1/2, 3/2-y, 1-z$ | 3.026 ( 7) | 2.29 (14) | 168 (14) |
| N(12)T1 | O(1)P2 | $x, y, z$ | 2.782 ( 7) | 1.91 (14) | 136 (11) |
| N(12)T1 | O(6')P2 | $x, y, z$ | 3.079 ( 8) | 2.18 (14) | 139 (10) |
| O(1)P1 | O(12)T1 | $x, y, z$ | 2.644 ( 8) | — | — |
| N(1)T2 | O(6')P2 | $x+1, y, z$ | 3.145 (10) | 2.56 (13) | 116 ( 9) |
| N(1)T2 | O(6)P2 | $x+1, y, z$ | 3.166 (11) | 2.41 (13) | 130 (10) |
| N(12)T2 | O(13)T1 | $x, y, z$ | 2.880 ( 7) | 2.14 (14) | 142 (12) |
| N(12)T2 | O(1)P2 | $x, y, z$ | 2.934 ( 7) | 2.51 (14) | 110 (11) |
| N(12)T2 | O(2)P2 | $x, y, z$ | 2.964 ( 8) | 2.12 (14) | 133 (11) |
| N(12)T2 | O(13)T1 | $x+1/2, 3/2-y, 1-z$ | 2.922 ( 7) | 2.04 (14) | 157 (13) |

*a)* The suffix letters T1, T2, P1 and P2 indicate two independent tryptophan and picric acid molecules, respectively.

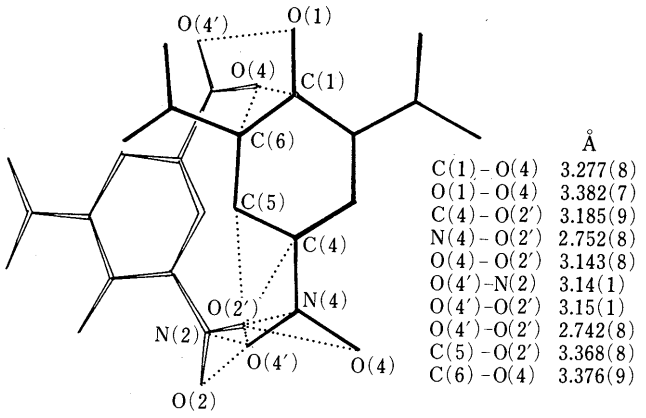


Fig. 4. Overlapping between Picric Acid Molecules Related by a Diad Screw Symmetry

Dotted lines show short contacts less than 3.4 Å.

with T2 or P2 polar atoms of pair II within respective reasonable distances. On the other hand, the $NH_3^+$ group of T2 molecule forms four hydrogen bonds or electrostatic interactions, and two of them are used for the linkage with pair I and the remains participate in the stabilization of stacking interaction with P2 molecule. As a whole, the amino and carboxyl groups of tryptophan, together with the nitro groups of picric acids, form an infinite hydrogen-bonded helical array around a diad screw axis. This packing mode is one of the most representative molecular packing patterns formed in the carboxylate complexes of amines.[13)]

The OH group of P1, as a neutral form, participates in the hydrogen bond with T1 O(12) atom. While the N(1) atom of T1 is singly hydrogen-bonded to the O(4) atom of neighboring P1, that of T2 is bifurcately hydrogen-bonded to two oxygen atoms of the P2 nitro group; this is a frequently observed pattern in the indole–picrate complexes.[7)]

Besides the indole–picric acid interaction (discussed later), a partial overlapping is formed between the P2 molecules related by a diad screw symmetry, as is shown in Fig. 4. The dihedral angle between them is 34.4(1)° and the short contacts are mainly formed between the polar nitro and/or phenol groups of respective molecules. This stacking appears to be stabilized by the electrostatic interactions of C(1) [0.2707*e*]–O(4) [−0.3834*e*], N4 [0.4672*e*]–O(2') [−0.4108*e*] and O(4') [−0.3762*e*]–N(2) [0.5024*e*].

**Stacking Interaction in Tryptophan–Picric Acid Complex** The stacking modes of the indole–picric acid in-

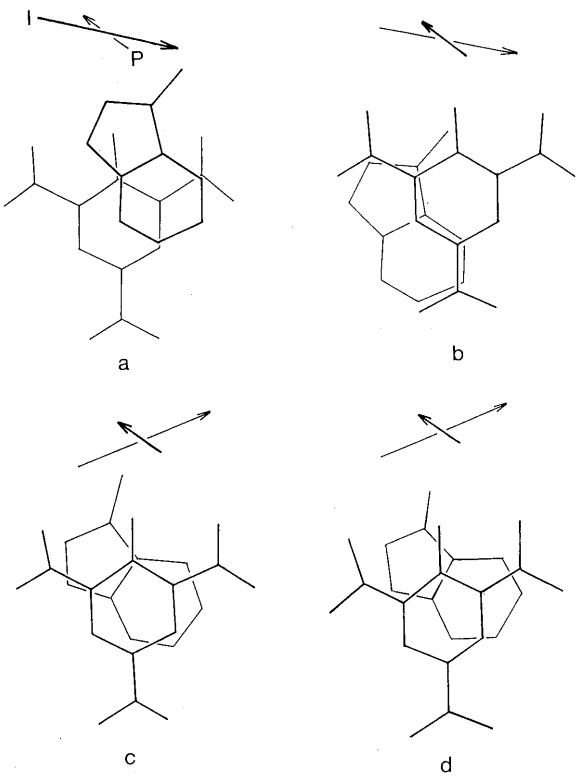


Fig. 5. Stacking Interaction Mode between Tryptophan Indole Ring and Picric Acid Benzene Moiety Observed in Upper (a) and Lower (b) Pairs of Indole Ring Relative to Central Picric Acid in Pair I, in Pair II (c) and in DL-Tryptophan–Picric Acid Crystal (d)

Arrows above each figure show the dipole moments of tryptophan indole ring (I) and picric acid (P).

teractions observed in the crystal are schematically shown in Fig. 5, together with that in DL-tryptophan picrate complex[7] for the comparison. Short contacts for respective stacking pairs are given in Table V. Present crystal structure revealed three kinds of stacking interaction modes of indole–picric acid aromatic rings. Pair I forms an infinite stacking column, in which both the aromatic rings are almost parallelly arranged with the dihedral angles of 2.9(3)° and the mean interplanar spacing is 3.46 Å for the upper pair of the indole ring (Fig. 5a) and 3.52 Å for the lower one (Fig. 5b) with respect to the central picric acid plane. On the other hand, pair II forms a 1 : 1 stacking complex of Fig. 5c, where the dihedral angle is 8.1(3)° and the mean interplanar spacing is 3.48 Å.

The geometries of stacked indole–picric acid pairs observed (Fig. 5a—c) are almost similar, and the relative orientation of the indole and picric acid rings in respective pairs differs mainly by the translation of the indole ring relative to the picric acid. The short contacts are formed at such atomic pairs that the nitro and/or hydroxyl groups of picric acid interact with the indole ring. The common stacking mode observed in pairs I and II, *i.e.*, the parallel alignment of indole–benzene rings with the interplanar spacing close to 3.4 Å (a minimum van der Waals separation distance between aromatic rings), is primarily formed by the $\pi$–$\pi$ charge-transfer interaction of both aromatic rings, in addition to the hydrogen bonds of O(1)P1$\cdots$O(12)T1 for pair I and N(12)T2$\cdots$O(1)P2 and $\cdots$O(2)P2 for pair II. This would be the essence of the red coloration of the

Table V. Stacking Short Contacts between Aromatic Rings Less than 3.5 Å

| | Atom 1 | Atom 2 | Distance (Å) |
|---|---|---|---|
| Pair I | T1 ($x$, $y$, $z$) | P1 ($x$, $y$, $z$) | |
| | N(1) | O(1) | 3.39 (1) |
| | C(2) | O(1) | 3.49 (1) |
| | C(4) | N(2) | 3.33 (1) |
| | C(4) | O(2′) | 3.44 (1) |
| | C(5) | O(2′) | 3.45 (1) |
| | C(6) | C(3) | 3.40 (1) |
| | C(8) | C(1) | 3.43 (1) |
| | T1 ($z$, $y$, $z$) | P1 ($x-1$, $y$,$z$) | |
| | C(2) | N(6) | 3.33 (1) |
| | C(2) | O(6′) | 3.19 (1) |
| | C(3) | C(6) | 3.42 (1) |
| | C(3) | O(6′) | 3.50 (1) |
| | C(4) | C(4) | 3.50 (1) |
| | C(5) | N(4) | 3.41 (1) |
| | C(5) | O(4) | 3.39 (1) |
| | C(9) | C(5) | 3.46 (1) |
| | C(10) | C(1) | 3.46 (1) |
| Pair II | T2 ($x$, $y$, $z$) | P2 ($x$, $y$, $z$) | |
| | C(2) | O(2) | 3.36 (1) |
| | C(4) | C(6) | 3.46 (1) |
| | C(4) | N(6) | 3.38 (1) |
| | C(4) | O(6′) | 3.45 (1) |
| | C(5) | C(5) | 3.42 (1) |
| | C(5) | N(6) | 3.49 (1) |
| | C(6) | C(5) | 3.31 (2) |
| | C(7) | C(4) | 3.40 (1) |

complex crystals. As is obvious from the direction of the dipole moments of the respective molecules, indicated by arrows above the respective figures, the orientation between the aromatic rings appears to be dominated by the dipole–dipole coupling of respective molecules, in addition to the indole HOMO–picric acid LUMO interaction. The stacking geometry of pair II is furthermore stabilized by the electrostatic interactions between the short contact atomic pairs: C(2) [0.0885$e$]–O(2) [$-$0.3489$e$], C(4) [$-$0.0378$e$]–N(6) [0.4932$e$], C(6) [$-$0.0013$e$]–C(5) [0.0730$e$] and C(7) [0.0073$e$]–C(4) [$-$0.0714$e$], and this would be attributable to the slight difference between the stacking modes of pairs I and II.

The stacking mode observed in DL-tryptophan picrate crystal is shown in Fig. 5d. It is important to note that this mode is quite identical with that of Fig. 5c, irrespective of different packing effects accompanied by the crystallization.[20] This means that the stacking mode shown in Fig. 5c reveals the most stable interaction intrinsic in the tryptophan–picric acid complex.

**References and Notes**

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