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(S)-Ethyl 1,2,3,9-tetrahydropyrrolo[2,1-b]quinazoline-1-carboxylate

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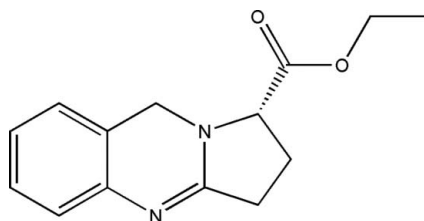
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 Key indicators: single-crystal X-ray study; $T = 187$ K; mean $\sigma(\text{C}-\text{C}) = 0.003$ Å; R factor = 0.032; wR factor = 0.076; data-to-parameter ratio = 7.6.

The title chiral compound, $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_2$, was prepared by esterification of (*S*)-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-1-carboxylic acid in the presence of HCl/EtOH. In the molecule, the quinazoline ring is non-planar and exhibits a distorted half-chair conformation, while the five-membered ring shows a typical envelope conformation. Intermolecular $\text{C}-\text{H}\cdots\text{N}$ hydrogen bonding helps to stabilize the crystal structure.

Related literature

 For general background, see: Cheng *et al.* (2006); Hua *et al.* (2002).


Experimental

Crystal data

$\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_2$
 $M_r = 244.29$
 Monoclinic, $P2_1$
 $a = 6.0545$ (8) Å
 $b = 9.1438$ (13) Å
 $c = 11.5228$ (16) Å
 $\beta = 92.905$ (2)°
 $V = 637.10$ (15) Å³
 $Z = 2$
 Mo $K\alpha$ radiation
 $\mu = 0.09$ mm⁻¹
 $T = 187$ (2) K
 $0.29 \times 0.22 \times 0.19$ mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
 Absorption correction: none
 3430 measured reflections
 1246 independent reflections
 1166 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.016$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.031$
 $wR(F^2) = 0.076$
 $S = 1.08$
 1246 reflections
 164 parameters
 1 restraint
 H-atom parameters constrained
 $\Delta\rho_{\text{max}} = 0.11$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.14$ e Å⁻³

Table 1

Hydrogen-bond geometry (Å, °).

| $D-\text{H}\cdots A$ | $D-\text{H}$ | $\text{H}\cdots A$ | $D\cdots A$ | $D-\text{H}\cdots A$ |
|--|--------------|--------------------|-------------|----------------------|
| $\text{C5}-\text{H5}\cdots\text{N2}^i$ | 0.95 | 2.59 | 3.523 (3) | 169 |

 Symmetry code: (i) $-x + 3, y + \frac{1}{2}, -z$.

Data collection: *SMART* (Bruker, 1997); cell refinement: *SAINTE* (Bruker, 1999); data reduction: *SAINTE*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL-Plus* (Sheldrick, 2008); software used to prepare material for publication: *SHELXL97*.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: XU2409).

References

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 Cheng, M.-S., Li, Q., Lin, B., Sha, Y., Ren, J.-H., He, Y., Wang, Q.-H., Hua, H.-M. & Kenneth, R. (2006). *Tetrahedron Asymmetry*, **17**, 179–183.
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supplementary materials

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(S)-Ethyl 1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazoline-1-carboxylate

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Comment

The title chiral compound is a derivate of (*S*)-1,2,3,9-tetrahydro-pyrrolo(2,1 - *b*)quinazolin-1-carboxylic acid (Linaria acid). Linaria acid is a nature compound, was isolated from the *Linaria vulgaris* (Hua *et al.*, 2002). *Linaria vulgaris* is a grassy plant that occurs in northeast China. The plant is used in traditional folk medicine for the treatment of coughs and asthma and as an expectorant. As part of our search on new Linaria acid derivate compounds (Cheng *et al.*, 2006), the title compound is recently synthesized and its crystal structure is reported here.

The molecular structure is shown in Fig. 1. The bond lengths and angles are within normal ranges. The quinazoline moiety is not planar, the central N-heterocyclic ring shows a distorted conformation, with atom N1 and C8 displaced by 0.420 Å and 0.257 Å from the mean plane defined by atoms C1/C2/C7/N2. The five-membered ring adopts an envelope conformation, with atom C10 deviating by 0.443 Å from the plane formed by the other atoms in the ring. Atom C11 of the title molecule is chiral, *S* configuration was assigned to this atom based on the known chirality of the equivalent atom in the starting material. An intermolecular C—H···N hydrogen bonding (Table 1) helps to stabilize the crystal structure.

Experimental

A rapid stream of hydrogen chloride was passed for 3 h into absolute ethanol (200 ml) in an icebath. To this solution was added (*S*)-1,2,3,9-tetrahydro-pyrrolo(2,1 - *b*)quinazolin-1-carboxylic acid (4.32 g, 20 mmol), and this solution was refluxed for 3 h. The ethanol was removed under vacuum. The pure product was obtained through silica gel chromatography (eluant: petroleum ether/ethyl acetate, 1:10). Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a dilute solution of the title compound in ethyl acetate at room temperature.

Refinement

All H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C—H = 0.95, 0.99, 0.98 and 1.00 Å for phenyl, methylene, methyl and tertiary H atoms, respectively, with $U_{\text{iso}}(\text{H}) = xU_{\text{eq}}(\text{C})$, where $x=1.5$ for methyl H, and $x=1.2$ for all other H atoms. Based on known chirality of the equivalent atom in the starting material, the *S* chirality at C11 was assigned. Friedel pairs were merged.

Figures

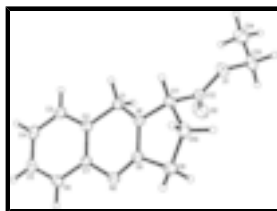


Fig. 1. The structure of the title compound, showing 30% probability displacement ellipsoids and the atom-numbering scheme.

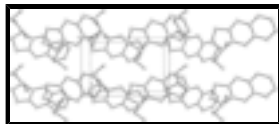


Fig. 2. The molecular packing of the title compound.

(S)-Ethyl 1,2,3,9-tetrahydropyrrolo[2,1-b]quinazoline-1-carboxylate

Crystal data

| | |
|---------------------------------|---|
| $C_{14}H_{16}N_2O_2$ | $F_{000} = 260$ |
| $M_r = 244.29$ | $D_x = 1.273 \text{ Mg m}^{-3}$ |
| Monoclinic, $P2_1$ | Mo $K\alpha$ radiation |
| Hall symbol: P 2yb | $\lambda = 0.71073 \text{ \AA}$ |
| $a = 6.0545 (8) \text{ \AA}$ | Cell parameters from 1588 reflections |
| $b = 9.1438 (13) \text{ \AA}$ | $\theta = 2.9\text{--}25.0^\circ$ |
| $c = 11.5228 (16) \text{ \AA}$ | $\mu = 0.09 \text{ mm}^{-1}$ |
| $\beta = 92.905 (2)^\circ$ | $T = 187 (2) \text{ K}$ |
| $V = 637.10 (15) \text{ \AA}^3$ | Block, colorless |
| $Z = 2$ | $0.29 \times 0.22 \times 0.19 \text{ mm}$ |

Data collection

| | |
|--|--|
| Bruker SMART APEX CCD area-detector diffractometer | 1166 reflections with $I > 2\sigma(I)$ |
| Radiation source: fine-focus sealed tube | $R_{\text{int}} = 0.016$ |
| Monochromator: graphite | $\theta_{\text{max}} = 25.4^\circ$ |
| $T = 187(2) \text{ K}$ | $\theta_{\text{min}} = 1.8^\circ$ |
| φ and ω scans | $h = -7 \rightarrow 7$ |
| Absorption correction: none | $k = -11 \rightarrow 5$ |
| 3430 measured reflections | $l = -13 \rightarrow 13$ |
| 1246 independent reflections | |

Refinement

| | |
|--|--|
| Refinement on F^2 | Secondary atom site location: difference Fourier map |
| Least-squares matrix: full | Hydrogen site location: inferred from neighbouring sites |
| $R[F^2 > 2\sigma(F^2)] = 0.031$ | H-atom parameters constrained |
| $wR(F^2) = 0.076$ | $w = 1/[\sigma^2(F_o^2) + (0.0381P)^2 + 0.082P]$ |
| $S = 1.08$ | where $P = (F_o^2 + 2F_c^2)/3$ |
| 1246 reflections | $(\Delta/\sigma)_{\text{max}} = 0.001$ |
| 164 parameters | $\Delta\rho_{\text{max}} = 0.11 \text{ e \AA}^{-3}$ |
| 1 restraint | $\Delta\rho_{\text{min}} = -0.14 \text{ e \AA}^{-3}$ |
| Primary atom site location: structure-invariant direct methods | Extinction correction: none |

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R -factors(gt) *etc.* and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

| | <i>x</i> | <i>y</i> | <i>z</i> | $U_{\text{iso}}^*/U_{\text{eq}}$ |
|------|------------|------------|--------------|----------------------------------|
| C1 | 0.8935 (4) | 0.4244 (2) | 0.24523 (19) | 0.0343 (5) |
| H1A | 0.9134 | 0.4636 | 0.3252 | 0.041* |
| H1B | 0.7364 | 0.4369 | 0.2188 | 0.041* |
| C2 | 1.0401 (3) | 0.5062 (2) | 0.16534 (17) | 0.0301 (5) |
| C3 | 0.9824 (4) | 0.6432 (3) | 0.12309 (18) | 0.0360 (5) |
| H3 | 0.8452 | 0.6850 | 0.1421 | 0.043* |
| C4 | 1.1216 (4) | 0.7206 (3) | 0.05344 (18) | 0.0403 (5) |
| H4 | 1.0813 | 0.8155 | 0.0263 | 0.048* |
| C5 | 1.3199 (4) | 0.6585 (3) | 0.02377 (18) | 0.0385 (5) |
| H5 | 1.4157 | 0.7105 | -0.0244 | 0.046* |
| C6 | 1.3781 (4) | 0.5209 (3) | 0.06430 (18) | 0.0348 (5) |
| H6 | 1.5135 | 0.4786 | 0.0430 | 0.042* |
| C7 | 1.2412 (3) | 0.4433 (2) | 0.13602 (16) | 0.0295 (5) |
| C8 | 1.1581 (3) | 0.2248 (3) | 0.22061 (16) | 0.0309 (5) |
| C9 | 1.1809 (4) | 0.0669 (3) | 0.2550 (2) | 0.0413 (6) |
| H9A | 1.2678 | 0.0565 | 0.3297 | 0.050* |
| H9B | 1.2532 | 0.0098 | 0.1946 | 0.050* |
| C10 | 0.9409 (4) | 0.0170 (3) | 0.2667 (2) | 0.0428 (6) |
| H10A | 0.9307 | -0.0560 | 0.3297 | 0.051* |
| H10B | 0.8795 | -0.0261 | 0.1931 | 0.051* |
| C11 | 0.8183 (3) | 0.1590 (3) | 0.29605 (17) | 0.0351 (5) |
| H11 | 0.6653 | 0.1587 | 0.2590 | 0.042* |
| C12 | 0.8108 (4) | 0.1795 (3) | 0.42708 (19) | 0.0387 (6) |
| C13 | 0.6211 (4) | 0.1044 (4) | 0.5926 (2) | 0.0562 (8) |
| H13A | 0.7692 | 0.1147 | 0.6322 | 0.067* |
| H13B | 0.5573 | 0.0102 | 0.6169 | 0.067* |
| C14 | 0.4776 (5) | 0.2258 (4) | 0.6279 (2) | 0.0595 (7) |
| H14A | 0.3311 | 0.2158 | 0.5886 | 0.089* |
| H14B | 0.5433 | 0.3193 | 0.6063 | 0.089* |
| H14C | 0.4636 | 0.2228 | 0.7123 | 0.089* |
| N1 | 0.9521 (3) | 0.2705 (2) | 0.24410 (14) | 0.0315 (4) |
| N2 | 1.3078 (3) | 0.3013 (2) | 0.17238 (15) | 0.0328 (4) |
| O1 | 0.6431 (3) | 0.1034 (2) | 0.46705 (14) | 0.0454 (4) |

supplementary materials

O2 0.9396 (3) 0.2508 (3) 0.48572 (14) 0.0652 (6)

Atomic displacement parameters (\AA^2)

| | U^{11} | U^{22} | U^{33} | U^{12} | U^{13} | U^{23} |
|-----|-------------|-------------|-------------|--------------|--------------|--------------|
| C1 | 0.0276 (11) | 0.0351 (13) | 0.0405 (11) | 0.0037 (10) | 0.0048 (9) | -0.0020 (10) |
| C2 | 0.0287 (10) | 0.0315 (12) | 0.0298 (10) | -0.0010 (9) | -0.0006 (8) | -0.0023 (9) |
| C3 | 0.0340 (11) | 0.0361 (12) | 0.0380 (11) | 0.0045 (10) | 0.0007 (9) | -0.0005 (10) |
| C4 | 0.0511 (14) | 0.0309 (12) | 0.0383 (11) | 0.0021 (11) | -0.0026 (10) | 0.0044 (11) |
| C5 | 0.0450 (12) | 0.0389 (13) | 0.0316 (11) | -0.0062 (11) | 0.0036 (9) | 0.0033 (10) |
| C6 | 0.0296 (10) | 0.0399 (13) | 0.0351 (11) | -0.0049 (10) | 0.0042 (9) | -0.0039 (11) |
| C7 | 0.0276 (10) | 0.0320 (12) | 0.0285 (10) | 0.0003 (9) | -0.0014 (8) | -0.0011 (9) |
| C8 | 0.0282 (10) | 0.0337 (11) | 0.0307 (10) | 0.0034 (10) | 0.0013 (8) | -0.0002 (9) |
| C9 | 0.0376 (12) | 0.0370 (14) | 0.0495 (14) | 0.0034 (11) | 0.0055 (10) | 0.0055 (10) |
| C10 | 0.0451 (14) | 0.0366 (13) | 0.0471 (13) | -0.0041 (11) | 0.0065 (11) | 0.0043 (11) |
| C11 | 0.0279 (10) | 0.0412 (13) | 0.0361 (11) | -0.0061 (10) | 0.0011 (8) | 0.0062 (10) |
| C12 | 0.0308 (11) | 0.0479 (15) | 0.0372 (11) | 0.0032 (10) | 0.0001 (9) | 0.0092 (10) |
| C13 | 0.0580 (16) | 0.073 (2) | 0.0391 (13) | 0.0063 (16) | 0.0170 (12) | 0.0200 (14) |
| C14 | 0.0631 (16) | 0.0670 (18) | 0.0495 (14) | -0.0021 (16) | 0.0120 (12) | -0.0016 (15) |
| N1 | 0.0274 (9) | 0.0328 (11) | 0.0347 (9) | 0.0008 (8) | 0.0050 (7) | 0.0042 (8) |
| N2 | 0.0260 (9) | 0.0347 (11) | 0.0380 (9) | 0.0017 (8) | 0.0046 (7) | 0.0019 (8) |
| O1 | 0.0442 (9) | 0.0514 (11) | 0.0418 (9) | -0.0038 (8) | 0.0140 (7) | 0.0093 (8) |
| O2 | 0.0519 (11) | 0.1046 (18) | 0.0385 (9) | -0.0257 (12) | -0.0036 (8) | 0.0003 (11) |

Geometric parameters (\AA , $^\circ$)

| | | | |
|-----------|-------------|--------------|-----------|
| C1—N1 | 1.452 (3) | C9—C10 | 1.536 (3) |
| C1—C2 | 1.509 (3) | C9—H9A | 0.9900 |
| C1—H1A | 0.9900 | C9—H9B | 0.9900 |
| C1—H1B | 0.9900 | C10—C11 | 1.541 (4) |
| C2—C3 | 1.383 (3) | C10—H10A | 0.9900 |
| C2—C7 | 1.403 (3) | C10—H10B | 0.9900 |
| C3—C4 | 1.387 (3) | C11—N1 | 1.450 (3) |
| C3—H3 | 0.9500 | C11—C12 | 1.524 (3) |
| C4—C5 | 1.387 (3) | C11—H11 | 1.0000 |
| C4—H4 | 0.9500 | C12—O2 | 1.199 (3) |
| C5—C6 | 1.381 (3) | C12—O1 | 1.332 (3) |
| C5—H5 | 0.9500 | C13—O1 | 1.459 (3) |
| C6—C7 | 1.394 (3) | C13—C14 | 1.480 (4) |
| C6—H6 | 0.9500 | C13—H13A | 0.9900 |
| C7—N2 | 1.416 (3) | C13—H13B | 0.9900 |
| C8—N2 | 1.293 (3) | C14—H14A | 0.9800 |
| C8—N1 | 1.355 (3) | C14—H14B | 0.9800 |
| C8—C9 | 1.502 (3) | C14—H14C | 0.9800 |
| N1—C1—C2 | 108.86 (17) | C9—C10—C11 | 103.7 (2) |
| N1—C1—H1A | 109.9 | C9—C10—H10A | 111.0 |
| C2—C1—H1A | 109.9 | C11—C10—H10A | 111.0 |
| N1—C1—H1B | 109.9 | C9—C10—H10B | 111.0 |

| | | | |
|------------|-------------|---------------|-------------|
| C2—C1—H1B | 109.9 | C11—C10—H10B | 111.0 |
| H1A—C1—H1B | 108.3 | H10A—C10—H10B | 109.0 |
| C3—C2—C7 | 119.57 (19) | N1—C11—C12 | 111.57 (19) |
| C3—C2—C1 | 121.18 (19) | N1—C11—C10 | 102.49 (17) |
| C7—C2—C1 | 119.23 (18) | C12—C11—C10 | 111.05 (18) |
| C2—C3—C4 | 121.1 (2) | N1—C11—H11 | 110.5 |
| C2—C3—H3 | 119.5 | C12—C11—H11 | 110.5 |
| C4—C3—H3 | 119.5 | C10—C11—H11 | 110.5 |
| C5—C4—C3 | 119.5 (2) | O2—C12—O1 | 125.1 (2) |
| C5—C4—H4 | 120.2 | O2—C12—C11 | 125.0 (2) |
| C3—C4—H4 | 120.2 | O1—C12—C11 | 109.86 (19) |
| C6—C5—C4 | 119.9 (2) | O1—C13—C14 | 111.2 (2) |
| C6—C5—H5 | 120.0 | O1—C13—H13A | 109.4 |
| C4—C5—H5 | 120.0 | C14—C13—H13A | 109.4 |
| C5—C6—C7 | 121.0 (2) | O1—C13—H13B | 109.4 |
| C5—C6—H6 | 119.5 | C14—C13—H13B | 109.4 |
| C7—C6—H6 | 119.5 | H13A—C13—H13B | 108.0 |
| C6—C7—C2 | 118.89 (19) | C13—C14—H14A | 109.5 |
| C6—C7—N2 | 118.26 (19) | C13—C14—H14B | 109.5 |
| C2—C7—N2 | 122.80 (18) | H14A—C14—H14B | 109.5 |
| N2—C8—N1 | 126.3 (2) | C13—C14—H14C | 109.5 |
| N2—C8—C9 | 125.2 (2) | H14A—C14—H14C | 109.5 |
| N1—C8—C9 | 108.43 (19) | H14B—C14—H14C | 109.5 |
| C8—C9—C10 | 103.55 (19) | C8—N1—C11 | 113.89 (18) |
| C8—C9—H9A | 111.0 | C8—N1—C1 | 121.87 (18) |
| C10—C9—H9A | 111.1 | C11—N1—C1 | 122.40 (17) |
| C8—C9—H9B | 111.1 | C8—N2—C7 | 115.34 (18) |
| C10—C9—H9B | 111.1 | C12—O1—C13 | 116.7 (2) |
| H9A—C9—H9B | 109.0 | | |

Hydrogen-bond geometry (\AA , $^\circ$)

| $D-H\cdots A$ | $D-H$ | $H\cdots A$ | $D\cdots A$ | $D-H\cdots A$ |
|--------------------|-------|-------------|-------------|---------------|
| $C5-H5\cdots N2^i$ | 0.95 | 2.59 | 3.523 (3) | 169 |

Symmetry codes: (i) $-x+3, y+1/2, -z$.

Fig. 1

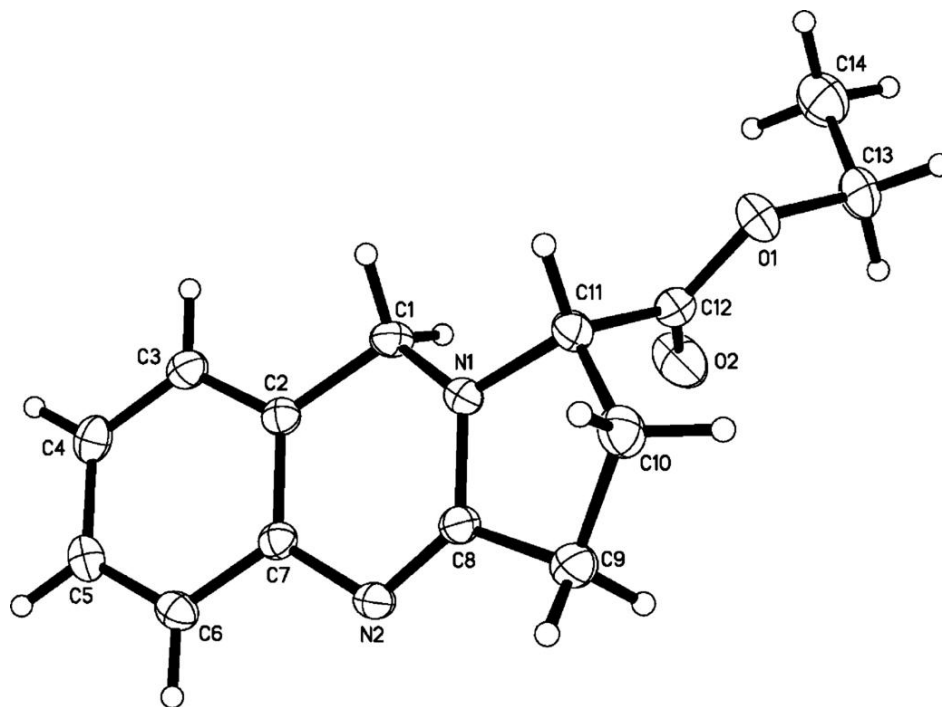


Fig. 2

