The title compound, \( \text{C}_{24}\text{H}_{26}\text{N}_{2}\text{O}_{8} \), is a derivative of neihumicin, a cytotoxic antibiotic from \( \text{Micromonospora neihuensis} \). The compound crystallizes as discrete molecules with crystallographic inversion symmetry. Intermolecular N–H⋯O hydrogen bonds yield polymeric chains along the \( c \) axis. The trimethoxyphenylmethylene side chain is found to be in a \( Z \) configuration about the \( \text{C}═\text{C} \) double bond.

**Comment**

\( \alpha,\beta \)-Unsaturated amino acid derivatives are present in many natural products, several of which exhibit biological properties. For example, neihumicin, produced by \( \text{Micromonospora neihuensis} \), is a cytotoxic antibiotic (Wu et al., 1988; Yang et al., 1988). A structure–activity relationship (SAR) of piperazine-2,5-dione derivatives of neihumicin has been carried out (Yokoi et al., 1988). We report here the first solid-state structural elucidation of the title compound, (I), a neihumicin derivative from the reported SAR study. Compound (I) was obtained by a modification of the procedure (Gallina & Liberatori, 1973) where 1,3-diacetyl piperazine-2,5-dione (Marcuccio & Elix, 1984) was condensed with 3,4,5-trimethoxybenzaldehyde in the presence of a strong base, namely potassium tert-butoxide.

The crystal structure of (I) consists of discrete molecules with a crystallographic centre of symmetry located at the centre of the pyrazine ring, such that the asymmetric unit consists of half the molecule (Fig. 1). The trimethoxyphenylmethylene side chain is found to be in the \( Z \) configuration about the \( \text{C}═\text{C} \) double bond. The molecules are linked along the \( c \) axis by an \( R_{2}^{2}(8) \) N–H⋯O interaction (Bernstein et al., 1995) between the amide and carbonyl oxygen groups (Table 2 and Fig. 2). This interaction presumably stabilizes the planar
Figure 1
View of the title compound, with the atom numbering scheme. Displacement ellipsoids for non-H atoms are drawn at the 50% probability level. H atoms are included with arbitrary radii. The symmetry code of the primed atoms is (1 − x, −y, 1 − z).

conformation of the piperazine ring. The C3−C4 and C1−C2 [symmetry code: (i) 1 − x, −y, 1 − z] distances of 1.466 (5) and 1.486 (5) Å are close to the value of 1.48 Å expected for a single bond between two sp2-hybridized C atoms (Allen et al., 1987). Analogous C3−C4 and/or C1−C2 bond lengths with intramolecular and intermolecular hydrogen-bond stabilization, respectively, have been observed with indolylidene piperazine-2,5-diones (Katritzky et al., 1989) and the cyclic dipeptide of dehydrophenylalanine (Ajo et al., 1985). The methoxy groups on atoms C6 and C8 are coplanar with the benzene ring. The group on C7, however, lies significantly out of the plane, with a C11−O3−C7−C8 angle of 69.4 (5)°. The benzene ring is twisted about the C3−C4 bond with respect to the piperazine ring, with a C2−C3−C4−C5 torsion angle of 37.3 (7)°.

Experimental
Potassium tert-butoxide (0.224 g, 2.00 mmol) in tert-butanol (2 ml) was added to a stirred solution of 3,4,5-trimethoxybenzaldehyde (0.392 g, 2.00 mmol) and 1,4-diacetylpiperazine-2,5-dione (0.4 g, 2.00 mmol) in dry DMF (4.0 ml) at 273 K. The mixture was stirred at room temperature for 24 h and worked up as described elsewhere (Gallina & Liberati, 1973), giving compound (I) as a yellow powder (329 mg, 35%). Yellow crystals of (I) [m.p. 529–530 K (decomposed); literature 528–529 K (Sonn, 1925) and 533–535 K (Yokoi et al., 1987)] were isolated by slow evaporation of a DMF solution of (I).1H NMR (200 MHz, CDCl3, p.p.m.): δH 8.25 (2H, brs, NH), 6.96 (2H, s, 1’-H), 6.59 [4H, s, o-C6H2(OCH3)2], 3.89 (18H, s, 6 × OCH3); ESMS− 469 (M−H−, 100%); ESMS+ 477 (MLi+, 70%).

Crystal data
C24H26N2O8
Mr = 470.47
Monoclinic, C2/c
a = 35.204 (3) Å
b = 5.282 (6) Å
c = 12.738 (4) Å
β = 97.503 (15)°
V = 2348 (3) Å³
Z = 4

Dx = 1.331 Mg m³
Mo Ka radiation
Cell parameters from 25 reflections
θ = 18.5–19.9°
µ = 0.10 mm⁻¹
T = 295 K
Plate, yellow
0.50 × 0.20 × 0.05 mm

Table 1
Selected geometric parameters (Å, °).

| O1−C1  | 1.229 (5)  | O4−C12 | 1.429 (6)  |
| O2−C6  | 1.365 (5)  | N1−C1  | 1.349 (5)  |
| O3−C7  | 1.365 (5)  | C1−C2  | 1.412 (4)  |
| O4−C8  | 1.362 (5)  | C3−C4  | 1.466 (5)  |
| C6−O2  | 1.296 (5)  | N1−C2  | 1.349 (5)  |
| C7−O3  | 1.156 (3)  | C2−C3  | 1.339 (5)  |
| O1−C1  | 1.209 (3)  | C3−C4  | 1.466 (5)  |
| O1−C1  | 1.213 (3)  | C4−C9  | 1.242 (4)  |
| N1−C2  | 1.257 (3)  | N1−C3  | 1.213 (3)  |

Symmetry code: (i) −x + 1, −y, −z + 1.

Table 2
Hydrogen-bond geometry (Å, °).

<table>
<thead>
<tr>
<th>D−H−A</th>
<th>D−H</th>
<th>H−A</th>
<th>D−A</th>
<th>D−H−A</th>
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</thead>
<tbody>
<tr>
<td>N1−H1−O1</td>
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<td>2.10</td>
<td>2.934 (5)</td>
<td>154</td>
</tr>
</tbody>
</table>

Symmetry code: (ii) −x + 1, −y, −z + 1.

H atoms were constrained as riding atoms, with C−H set to 0.95 Å. Ueq(H) values were set to 1.2Ueq of the parent atom.

Data collection: MSCI/AFC7 Diffractometer Control Software (Molecular Structure Corporation, 1999); cell refinement: MSCI/AFC7 Diffractometer Control Software.
AFC7 Diffractometer Control Software; data reduction: TExSAN for Windows (Molecular Structure Corporation, 2001); program(s) used to solve structure: TExSAN for Windows; program(s) used to refine structure: TExSAN for Windows and SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEP-3 (Farrugia, 1997); software used to prepare material for publication: TExSAN for Windows and PLATON (Spek, 2003).

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References