The title compound, \( \text{C}_{24}\text{H}_{26}\text{N}_{2}\text{O}_{8} \), is a derivative of neihumicin, a cytotoxic antibiotic from \( \textit{Micromonospora neihuensis} \). The compound crystallizes as discrete molecules with crystallographic inversion symmetry. Intermolecular N-H\cdots O hydrogen bonds yield polymeric chains along the \( c \) axis. The trimethoxyphenylmethylene side chain is found to be in a \( Z \) configuration about the \( \text{C} \equiv \text{C} \) 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 \( \textit{Micromonospora neihuensis} \), 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 \( \text{C} \equiv \text{C} \) double bond. The molecules are linked along the \( c \) axis by an \( R_2^2(8) \) N-H\cdots O interaction (Bernstein et al., 1995) between the amide and carbonyl oxygen groups (Table 2 and Fig. 2). This interaction presumably stabilizes the planar
conformation of the piperazine ring. The C3—C4 and C1—C2 i
symmetry code of the primed atoms is (1 + x, −y, 1 − z).

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-diacytelylpiperazine-2,5-dione (0.4 g, 2.0 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); 61, o1443–o1445 (329 mg, 35%)]. Yellow crystals of (I) were isolated by slow evaporation of a DMF solution of (I). 1HN M R
literature 528–529 K (Sonn, 1925) and 533–535 K (Yokoi et al., 1988) 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 (M+H+, 70%).

Crystal data
C24H26N2O8
M_r = 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

$D_0 = 1.331 \text{ Mg m}^{-3}$
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

Data collection
Rigaku AFC-7R diffractometer $\theta_{max} = 25.0°$
ω-2θ scans $h = 0 \rightarrow 41$
Absorption correction: none $k = 0 \rightarrow 6$
2106 measured reflections $l = -15 \rightarrow 15$
2070 independent reflections 3 standard reflections
1096 reflections with $I > 2\sigma(I)$

Refinement
Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.052$
wR($F^2$) = 0.189
$S = 1.03$
2070 reflections 154 parameters
H-atom parameters constrained

Table 1
Selected geometric parameters (Å, °).

|          | O1—C1   | O4—C12  | O2—C6   | O1—C1   | O4—C12  |
|----------|---------|---------|---------|---------|---------|
| D—H—A   | 1.229 (5)| 1.429 (6)| 1.365 (5)| 1.426 (6)| 1.365 (5)|
| D—H—A   | C1—C2   | C3—C4   | C1—C2   | C3—C4   | C1—C2   |
| O1—C1   | 1.425 (6)| 1.365 (5)| 1.229 (5)| 1.425 (6)| 1.365 (5)|
| D—H—A   | O1—C1   | C1—C2   | O1—C1   | C1—C2   | O1—C1   |
| N1—O1   | 1.425 (6)| 1.365 (5)| 1.229 (5)| 1.425 (6)| 1.365 (5)|
| D—H—A   | N1—O1   | C1—C2   | N1—O1   | C1—C2   | N1—O1   |
| O4—C8   | 1.436 (5)| 1.375 (5)| 1.429 (6)| 1.426 (6)| 1.365 (5)|
| D—H—A   | O4—C8   | C3—C4   | O4—C8   | C3—C4   | O4—C8   |
| C6—O2   | 1.175 (3)| 1.256 (3)| 1.181 (3)| 1.256 (3)| 1.181 (3)|
| D—H—A   | C6—O2   | C7—C8   | C6—O2   | C7—C8   | C6—O2   |
| C7—O3   | 1.156 (3)| 1.256 (3)| 1.181 (3)| 1.256 (3)| 1.181 (3)|
| D—H—A   | C7—O3   | C8—C9   | C7—O3   | C8—C9   | C7—O3   |
| C1—N1   | 1.178 (3)| 1.256 (3)| 1.181 (3)| 1.256 (3)| 1.181 (3)|
| D—H—A   | C1—N1   | C2—C3   | C1—N1   | C2—C3   | C1—N1   |
| C1—C2   | 1.209 (3)| 1.256 (3)| 1.256 (3)| 1.256 (3)| 1.256 (3)|
| D—H—A   | C1—C2   | C2—C3   | C1—C2   | C2—C3   | C1—C2   |
| C1—C1   | 1.121 (3)| 1.256 (3)| 1.256 (3)| 1.256 (3)| 1.256 (3)|
| D—H—A   | C1—C1   | C2—C3   | C1—C1   | C2—C3   | C1—C1   |
| C1—C1   | 1.257 (3)| 1.256 (3)| 1.256 (3)| 1.256 (3)| 1.256 (3)|
| D—H—A   | C1—C1   | C2—C3   | C1—C1   | C2—C3   | C1—C1   |

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

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

Data collection: MSC/AFC7 Diffractometer Control Software (Molecular Structure Corporation, 1999); cell refinement: MSC/
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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