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Key indicators

Single-crystal X-ray study
 T = 295 K
 Mean $\sigma(\text{C}-\text{C}) = 0.005 \text{ \AA}$
 R factor = 0.051
 wR factor = 0.145
 Data-to-parameter ratio = 7.4

For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

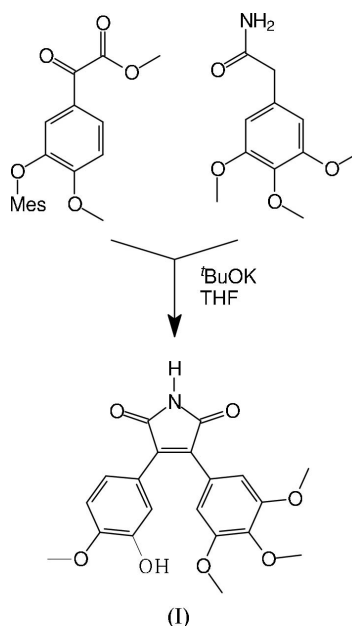
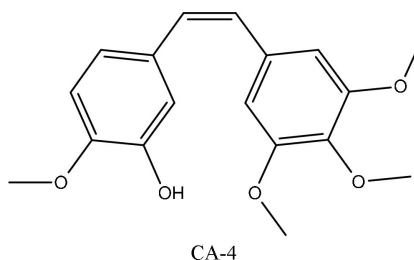
4-(3-Hydroxy-4-methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)-2,5-dihydro-1H-pyrrole-2,5-dione

The title compound, $\text{C}_{20}\text{H}_{19}\text{NO}_7$, crystallizes in the space group $Pna2_1$. X-ray analysis shows the compound has the desired 3'-hydroxy and 4'-methoxy substitution pattern, as in the natural template combretastatin A-4.

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Comment

The title compound, (I), bearing the maleimide (1H-pyrrole-2,5-dione) moiety as a core structure, was prepared in an effort to synthesize analogues of combretastatin A-4 (CA-4, see scheme), a well known antithrombotic compound (Woods *et al.*, 1995).



To study the concept of combining CA-4 and maleimide, compound (I) has been synthesized. Among the number of synthetic methods for preparing asymmetrical 3,4-diaryl-maleimides, the method of Faul *et al.* (1999) can be used

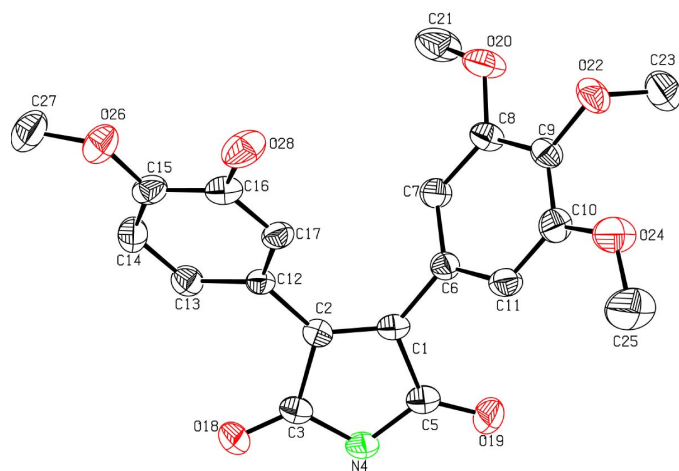


Figure 1
ORTEP view (Johnson, 1976) of the molecule of (I). Displacement ellipsoids are shown at the 50% probability level. H atoms have been omitted for clarity.

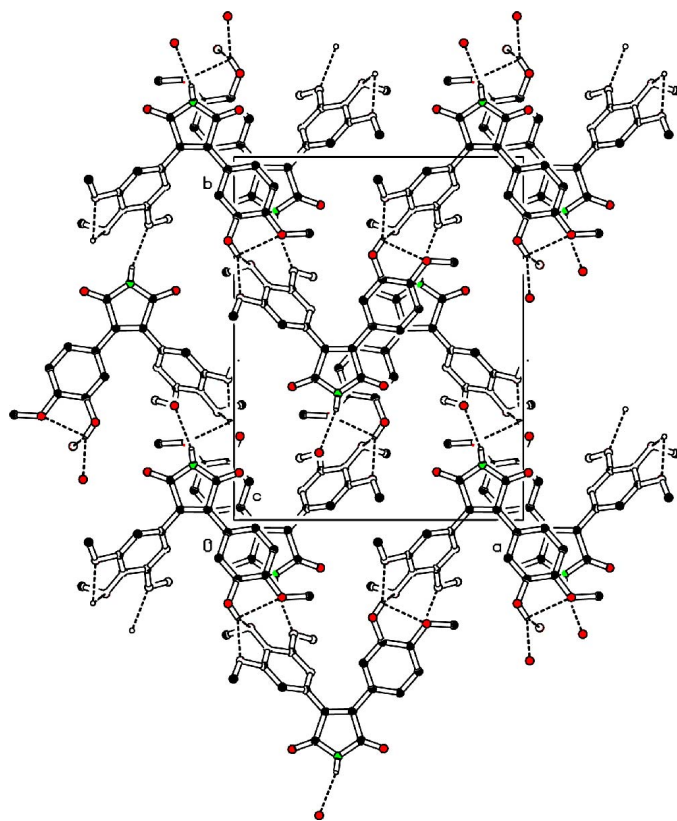


Figure 2
Packing diagram of (I), viewed along the *c* axis, showing the hydrogen bonds (dashed lines). H atoms not involved in hydrogen bonding have been omitted.

conveniently. Asymmetrically substituted 3,4-diarylmaleimides were prepared by one-pot condensation of an arylacetamide unit with aryl glyoxyl methyl ester using KO^tBu in tetrahydrofuran. According to this concept, methyl (3-methylsulfonyl-4-methoxyphenyl)glyoxalate was condensed with 3,4,5-trimethoxyphenylacetamide (see *Experimental* and reaction scheme).

We report here the X-ray crystal structure analysis of (I), which definitively confirms the structure. In the crystal structure, the combination of intermolecular $\text{N}-\text{H}\cdots\text{O}$ and $\text{O}-\text{H}\cdots\text{O}$ hydrogen bonds forms sheets parallel to the *bc* plane (Table 1 and Fig. 2).

Experimental

For synthesis of maleimide (I) the general procedure (Faul *et al.*, 1999) was followed using 3-methylsulfonyl-4-methoxyphenylmethylglyoxalate (1.50 g, 5.2 mmol), 3,4,5-trimethoxyphenylacetamide (1.13 g, 5.02 mmol) and 1.0 M KO^tBu (20 ml, 20.0 mmol) in tetrahydrofuran. We found that it was not necessary to remove the mesylate from the precursor 3-methylsulfonyl-4-methoxyphenylmethylglyoxalate prior to the formation of the maleimide. When using four equivalents of KO^tBu the mesyl group was cleaved simultaneously to the reaction yielding the maleimide moiety, and compound (I) showing the free phenolic function was obtained directly. Purification was achieved by column chromatography (ethyl acetate/hexanes 1:1) to yield (I) (0.85 g, 44%) as a yellow solid. Crystals of (I) precipitated at 278 K from ethanol solution by slow evaporation.

Crystal data

$\text{C}_{20}\text{H}_{19}\text{NO}_7$
 $M_r = 385.22$
Orthorhombic, $Pna2_1$
 $a = 14.0827$ (17) Å
 $b = 17.674$ (3) Å
 $c = 7.2238$ (4) Å
 $V = 1798.0$ (4) Å³
 $Z = 4$
 $D_x = 1.424$ Mg m⁻³

Cu $K\alpha$ radiation
Cell parameters from 25 reflections
 $\theta = 21\text{--}28^\circ$
 $\mu = 0.92$ mm⁻¹
 $T = 295$ (2) K
Needle, green–yellow
 $0.58 \times 0.12 \times 0.04$ mm

Data collection

Enraf–Nonius CAD-4 diffractometer
 $\theta/2\omega$ scans
Absorption correction: numerical (de Meulenaer & Tompa, 1965)
 $T_{\min} = 0.69$, $T_{\max} = 0.965$
3459 measured reflections
1972 independent reflections
1654 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.135$
 $\theta_{\max} = 74.0^\circ$
 $h = -17 \rightarrow 17$
 $k = -22 \rightarrow 21$
 $l = -8 \rightarrow 8$
3 standard reflections
frequency: 60 min
intensity decay: 3%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.051$
 $wR(F^2) = 0.145$
 $S = 1.07$
1972 reflections
268 parameters

Only H-atom U 's refined
 $w = 1/[\sigma^2(F_o^2) + (0.0712P)^2]$
where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} < 0.001$
 $\Delta\rho_{\max} = 0.44$ e Å⁻³
 $\Delta\rho_{\min} = -0.23$ e Å⁻³

Table 1
Hydrogen-bonding geometry (Å, °).

$D-\text{H}\cdots A$	$D-\text{H}$	$\text{H}\cdots A$	$D\cdots A$	$D-\text{H}\cdots A$
$\text{N4}-\text{H4}\cdots\text{O20}^i$	0.78	2.28	3.045 (4)	164
$\text{O28}-\text{H28}\cdots\text{O24}^{ii}$	0.91	2.10	2.909 (4)	146
$\text{O28}-\text{H28}\cdots\text{O22}^{ii}$	0.91	2.42	3.101 (5)	131

Symmetry codes: (i) $\frac{1}{2} - x, y - \frac{1}{2}, \frac{1}{2} + z$; (ii) $x - \frac{1}{2}, \frac{1}{2} - y, z$.

H atoms were placed in calculated positions, with C–H distances ranging from 0.93 to 0.96 Å and N–H = 0.78 Å. In the absence of significant anomalous dispersion effects, Friedel pairs were merged before the final cycles of refinement.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *CORINC* (Dräger & Gattow, 1971); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97*.

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