

Dimethyl 2-[[2-(methoxycarbonyl)-1-(methoxycarbonylmethyl)pyrrol-4-yl]-methylene]propanedioate

Jan Lokaj,^a Viktor Kettmann,^{b*} Viktor Milata,^a Pavol Hodul,^a Peter Kottaš^a and Ognyan Petrov^c

^aFaculty of Chemical Technology, Slovak Technical University, Radlinskeho 9, Bratislava 81237, Slovak Republic, ^bFaculty of Pharmacy, Comenius University, Odbojarov 10, Bratislava 83232, Slovak Republic, and ^cDepartment of Organic Chemical Technology, Faculty of Chemistry, University of Sofia, Sofia 1126, Bulgaria
Correspondence e-mail: kettmann@fpharm.uniba.sk

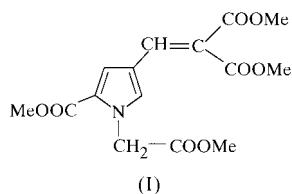
Received 27 February 2001

Accepted 15 May 2001

The title compound, C₁₅H₁₇NO₈, is a pyrrole–ethene derivative with potential biological activity. Although a large part of the molecule is planar, there is no structural evidence for any conjugation push–pull effect across the ethylenic bond, which is usually observed for substituted ethylenes; π -electron delocalization appears to be restricted to the 2-(methoxycarbonyl)pyrrole moiety.

Comment

Over the last decade, 2-(alkoxycarbonyl)pyrrole derivatives have attracted considerable interest as they display a broad spectrum of biological activities, the analgesic, morphine-agonist, spasmolytic, antipyretic and anti-inflammatory properties being some of the most important (Gribble, 1996). Recently, it has been reported that introduction of additional alkoxycarbonyl group(s) to the 4- and/or 1-position of the pyrrole ring has a favourable effect on the spasmolytic activity. Therefore, our strategy was to incorporate extra 2,2-bis-(methoxycarbonyl)vinyl and methoxycarbonylmethyl substituents in the 4- and 1-positions of the parent 2-(methoxycarbonyl)pyrrole in order to design novel compounds possessing spasmolytic and possibly other types of biological activity. Moreover, the title molecule, (I), can also be regarded



as a push–pull ethylene, a class of compounds exhibiting a variable degree of conjugation across the C=C double bond and also an associated polarization of the molecule, which is responsible for some unique properties of the compounds (e.g. absorption in the near-ultraviolet and visible regions). Thus,

the purpose of this X-ray structural analysis was twofold: (i) to determine the spatial distribution of the functional groups as one of the main determinants of the biological activity, and (ii) to assess the extent of conjugation for the future study of the relationship between the electronic and physicochemical properties of this class of compounds.

The title molecule along with the atom-numbering scheme is illustrated in Fig. 1. As expected, the central pyrrole ring is planar within experimental error [r.m.s. deviation 0.007 (2) Å] and is nearly coplanar with the plane of the ethylenic (C15=C16) bond [dihedral angle 8.8 (1)°]. The twist about the C=C bond, as measured by the angle between the planes through C4/C15/H15 and C16/C17/C21, is 2.3 (1)°. As shown by the torsion angles in Table 1, the ester group O22/C21/O23/C24 is approximately coplanar with the C=C double bond, while the other, oriented *Z* to the pyrrolyl ring, is almost perpendicular to the C=C plane, obviously attributable to steric collision with the heterocyclic ring. As for the other pyrrole substituents, the methoxycarbonyl group at C2 is also essentially coplanar with the pyrrole plane [dihedral angle 3.8 (1)°] and the methoxycarbonyl group O8/C7/O9/C10 is rotated around the N1–C6 and C6–C7 bonds so that it makes an angle of 72.5 (4)° with the plane of the pyrrole ring.

Although the pyrrole ring and one of the ester groups at C16 are coplanar with the ethylenic plane, there is no conjugation push–pull effect across the C=C double bond, as shown by the C15=C16 bond distance [1.334 (4) Å], which corresponds to the value of 1.336 (2) Å observed in unpolarized ethylene (Bartell *et al.*, 1965). Similarly, the C16–C17 and C16–C21 bond lengths of 1.513 (4) and 1.494 (4) Å, respectively, are in good agreement with the value of 1.487 (5) Å found for a pure *Csp*²–*Csp*² single bond (Shmueli *et al.*, 1973). The absence of polarization across the ethylenic bond explains the lack of colour in the compound. Nevertheless, on the other side of the molecule, some effect of the methoxycarbonyl group (at C2) on the π -electron distribution of the pyrrole ring is visible in the shortening of the C2–C11 bond distance (Table 1) with respect to the value given above

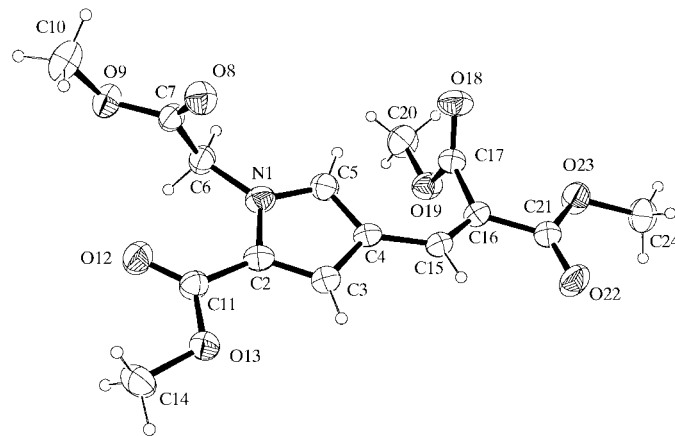


Figure 1
A view of the title molecule showing the labelling of the non-H atoms. Displacement ellipsoids are shown at the 30% probability level and H atoms are drawn as small circles of arbitrary radii.

for the Csp^2-Csp^2 single bond, and also in the non-equivalency of the two N–C bonds within the heterocyclic ring. Other bond lengths and angles within the pyrrole ring agree well with those found for unsubstituted pyrrole (Nygaard *et al.*, 1969).

Experimental

To a stirred solution of methyl (4-formyl-2-methoxycarbonylpyrrolyl)acetate (10 mmol) prepared previously (Lokaj *et al.*, 2001) in 20 ml of *N,N*-dimethylformamide (DMF) was added at once sodium dimethylmalonate (prepared freshly from dimethylmalonate and sodium hydride) in 15 ml of DMF. The reaction was quickly quenched with a saturated aqueous solution of ammonium chloride, extracted with diethyl ether, dried with sodium sulfate and evaporated to dryness. The remaining dimethylmalonate was then evaporated using a high-vacuum pump (0.1 Pa) and the residue crystallized from diethyl ether/*n*-pentane (m.p. 410–412 K).

Crystal data

$C_{15}H_{17}NO_8$
 $M_r = 339.30$
 Monoclinic, $P2_1/n$
 $a = 9.906(4) \text{ \AA}$
 $b = 12.528(5) \text{ \AA}$
 $c = 13.991(5) \text{ \AA}$
 $\beta = 105.44(4)^\circ$
 $V = 1673.7(11) \text{ \AA}^3$
 $Z = 4$
 $D_x = 1.347 \text{ Mg m}^{-3}$
 $D_m = 1.35(1) \text{ Mg m}^{-3}$

D_m measured by flotation in bromoform/cyclohexane
 Mo $K\alpha$ radiation
 Cell parameters from 15 reflections
 $\theta = 8-17^\circ$
 $\mu = 0.11 \text{ mm}^{-1}$
 $T = 293(2) \text{ K}$
 Plate, colourless
 $0.35 \times 0.30 \times 0.10 \text{ mm}$

Data collection

Syntex $P2_1$ diffractometer
 $\theta/2\theta$ scans
 3064 measured reflections
 2883 independent reflections
 1837 reflections with $I > 2\sigma(I)$
 $R_{int} = 0.037$
 $\theta_{max} = 25.0^\circ$

$h = -11 \rightarrow 0$
 $k = -14 \rightarrow 0$
 $l = -16 \rightarrow 16$
 2 standard reflections every 98 reflections
 intensity decay: 2%

Refinement

Refinement on F^2
 $R(F) = 0.059$
 $wR(F^2) = 0.197$
 $S = 1.00$
 2883 reflections
 221 parameters

H atom parameters constrained
 $w = 1/[\sigma^2(F_o^2) + (0.1083P)^2]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{max} = 0.002$
 $\Delta\rho_{max} = 0.23 \text{ e \AA}^{-3}$
 $\Delta\rho_{min} = -0.18 \text{ e \AA}^{-3}$

Most H atoms were seen in a difference Fourier map; all H atoms were refined with fixed geometry, riding on their carrier atoms, with U_{iso} set to 1.2 (or 1.5 for the methyl H atoms) times U_{eq} of the parent atom. The methyl groups were allowed to rotate about their local threefold axis.

Table 1

Selected geometric parameters (\AA , $^\circ$).

N1–C5	1.358 (4)	C4–C5	1.394 (4)
N1–C2	1.420 (4)	C4–C15	1.451 (4)
N1–C6	1.470 (3)	C15–C16	1.334 (4)
C2–C3	1.366 (4)	C16–C21	1.494 (4)
C2–C11	1.462 (4)	C16–C17	1.513 (4)
C3–C4	1.433 (4)		
C5–N1–C2	109.0 (2)	C5–C4–C15	129.3 (2)
C5–N1–C6	124.8 (2)	C3–C4–C15	124.8 (2)
C2–N1–C6	126.2 (2)	N1–C5–C4	109.3 (2)
C3–C2–N1	106.7 (3)	C16–C15–C4	129.6 (3)
C3–C2–C11	131.4 (3)	C15–C16–C21	119.1 (2)
N1–C2–C11	121.9 (3)	C15–C16–C17	123.2 (3)
C2–C3–C4	109.2 (2)	C21–C16–C17	117.7 (2)
C5–C4–C3	105.8 (2)		
C2–N1–C6–C7	70.1 (3)	C4–C15–C16–C17	2.7 (5)
N1–C6–C7–O8	22.4 (4)	C15–C16–C17–O18	91.5 (4)
N1–C2–C11–O12	–2.9 (5)	C15–C16–C21–O22	6.0 (5)
C5–C4–C15–C16	–8.3 (5)		

Data collection: *Syntex Software* (Syntex, 1973); cell refinement: *Syntex Software*; data reduction: *XP21* (Pavelčík, 1987); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97*.

This work was supported by the Grant Agency of the Slovak Republic, project Nos. 1/8216/01 and 1/6095/99.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1455). Services for accessing these data are described at the back of the journal.

References

- Bartell, L. C., Roth, E. A., Hollowell, C. D., Kuchitsu, K. & Young, J. E. (1965). *J. Chem. Phys.* **42**, 2683–2686.
- Gribble, G. W. (1996). *Pyrroles and their Benzo Derivatives: Applications*. In *Comprehensive Heterocyclic Chemistry II*, Vol. 2, edited by A. R. Katritzky, C. V. Rees & E. F. V. Scriven, ch. 2.04. Amsterdam: Elsevier.
- Johnson, C. K. (1976). *ORTEPII*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
- Lokaj, J., Kettmann, V., Milata, V., Štetinová, J. & Petrov, O. (2001). *Acta Cryst.* **E57**, o404–405.
- Nygaard, L., Nielsen, J. T., Kirchner, J., Maltesen, G., Rastrup-Anderson, J. & Sorensen, G. O. (1969). *J. Mol. Struct.* **3**, 491–500.
- Pavelčík, F. (1987). *XP21*. Comenius University, Slovakia.
- Sheldrick, G. M. (1990). *SHELXS97*. University of Göttingen, Germany.
- Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.
- Shmueli, U., Shanan-Atidi, H., Horwitz, H. & Shvo, Y. (1973). *J. Chem. Soc. Perkin Trans. 2*, pp. 657–662.
- Syntex (1973). *Syntex Software*. Syntex Analytical X-ray Instruments Inc., California, USA.