

electron density, as determined with X-rays, and that which would arise from 'free' spherical atoms placed at the nuclear positions determined with neutrons. A relevant scale factor was refined using Hanic's X-ray data and the neutron-determined (Table 1) structural parameters. Surfeits of electron density can be seen in Fig. 3 near the marked positions of all three oxygen nuclei and these may be attributed to 'lone pair' electron density. In particular, this excess density for O(2) is placed about the *intermolecular* bond O(2)···H(12) such that it impinges upon the path of O(2)—H(12). This, together with an apparent deficit of electrons in Fig. 3 around the marked position of the H(12) proton, could explain the possibility of obtaining a short value for the O(2)—H(12) bond lengths with X-rays. Indeed, Hanic (1968) placed the centre of the H(12) electron cloud 0.2 Å nearer O(2) than the present neutron-determined position of its proton. The magnitude of this discrepancy between neutron and X-ray scattering centres is similar to that found for hydrogen atoms in other compounds, such as in α -oxalic acid dihydrate and *sym*-triazine (Coppens, Sabine, Delaplane & Ibers, 1969).

Fig. 3 displays surfeits of electron density near the middle of most bonds, as well as near the electro-negative Cl atom. The maximum surfeit of electron density in Fig. 3 occurs near the Cl atom and equals $1.4 \text{ e } \text{Å}^{-3}$, which is about 10% of the full density arising at that point. The maximum excess electron density in the pyridine ring is $0.6 \text{ e } \text{Å}^{-3}$, which is about 10% of the maximum full density arising at the centre of each C atom. There is hardly any significant evidence, however, that excess electrons congregate near the N atom of the pyridine ring, any more than near C(3) for example.

In a further re-assessment of Hanic's X-ray data, all the atomic parameters were fixed at their neutron-

determined values (Table 1) and site-occupancy factors alone were refined, just for the hydrogen atoms. This gave rise to a slight decrease in $R(F)$ from 17.2 to 17.0% and to occupancy values 1.2 (1), 0.7 (1), 1.1 (1), 0.4 (1), 0.7 (1), 0.4 (1), 1.2 (1), 0.5 (1), 0.0 (1), 0.9 (1), 0.9 (1), 0.4 (1) for the atoms H(1) to H(12). Although any detailed attempt at interpretation of these results seems inappropriate, there is a general indication that the hydrogen atoms do not all possess a whole 1s electron. For example, H(4) and H(12), which moved appreciably in the present X-ray positional re-appraisal, have assumed condensed 1s electron clouds that seem, on the basis of this re-assessment, to be less than half full.

We are grateful to the Science Research Council and the Institut Laue-Langevin for providing the means of carrying out these experiments and the former for supporting one of us (JSP) with a postdoctoral award during the early stages of this work.

References

- COPPENS, P., SABINE, T. M., DELAPLANE, R. G. & IBERS, J. A. (1969). *Acta Cryst.* **B25**, 2451–2458.
 HANIC, F. (1966). *Acta Cryst.* **21**, 332–340.
 HANIC, F. (1968). *Chem. Zvesti.* **22**, 838–843.
 JOHNSON, C. (1970). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
 SHELDRICK, G. M. (1976). *SHELX 76*. A program for crystal-structure determination. Univ. of Cambridge, England.
 STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
 XRAY 72 (1972). Computer Science Center, Univ. of Maryland, College Park, Maryland.

Acta Cryst. (1980). **B36**, 1136–1141

A Comparison of the Structures of Three Substituted 2-Benzoylpyrroles

BY ROBIN B. ENGLISH,* GEORGE MCGILLIVRAY AND IN PART ELMA SMAL

Department of Chemistry, University of South Africa, PO Box 392, Pretoria, South Africa

(Received 1 November 1979; accepted 2 January 1980)

Abstract

The structures of 2-benzoylpyrrole (BZP), 2-(4-chlorobenzoyl)pyrrole (CLBZP) and 2-(4-methoxybenzoyl)-

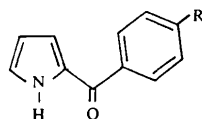
pyrrole (MEBZP) are described. BZP crystallizes in space group $P\bar{1}$ with $a = 10.687(5)$, $b = 10.623(5)$, $c = 3.953(5)$ Å, $\alpha = 98.35(1)$, $\beta = 98.38(1)$, $\gamma = 98.11(1)^\circ$, $Z = 2$. CLBZP and MEBZP crystallize in space groups $P2_1/n$ and $P2_1/c$ respectively: for CLBZP $a = 11.760(5)$, $b = 21.077(5)$, $c = 3.919(5)$

* To whom correspondence should be addressed.

\AA , $\beta = 98.08 (1)^\circ$ and for MEBZP $a = 11.784 (5)$, $b = 14.394 (5)$, $c = 6.083 (5) \text{\AA}$, $\beta = 102.74 (1)^\circ$. $Z = 4$ for both compounds. The structures were refined to $R = 0.054$ for BZP, 0.049 for CLBZP and 0.081 for MEBZP. The structures exhibit certain gross similarities: in all three the pyrrole ring and carbonyl group are coplanar and the phenyl ring is twisted out of this plane by between 45 and 52° . This degree of twist appears to be independent of the nature of the substituent in the benzene ring. The carbonyl groups are *cis* with regard to the N atom, and the structures consist of layers of hydrogen-bonded (*via* N—H and carbonyl O) centrosymmetrically related pairs of molecules. Bond lengths and angles in the molecules reveal differences which may be ascribed to benzene-ring substitution. Some π interaction is observed between the methoxy group and the benzene ring in MEBZP.

Introduction

Several detailed conformational studies of pyrroles containing a 2-carbonyl substituent have been carried out [see, for example, Bertin, Garbay-Jaureguiberry, Liegeois & Lumbroso (1976) and John, Ritchie & Radom (1977), and references quoted therein]. However, these studies have mainly concerned systems in which there is no steric resistance to the molecule's adopting a planar conformation, favoured by the strong conjugation between the carbonyl group and the pyrrole ring. In such compounds, the preference is for the carbonyl group to lie *cis* to the adjacent C—N bond. In 2-arylpyrroles which are the subject of this paper (Fig. 1) planarity is inhibited by steric interaction between the C(3)—H (present nomenclature) in the pyrrole ring and the *ortho* H atoms in the phenyl ring. As conjugation is possible between the carbonyl group and both the pyrrole and the phenyl rings in these compounds, they present a special case. Infrared studies (Kahn & Morgan, 1964) have indicated that the carbonyl group is not coplanar with the phenyl ring. More recently, Cheng, John, Ritchie & Gore (1974) have made a detailed study of the conformation of 2-benzoylpyrrole, BZP, by analysing dipole moments and molar Kerr constants. They considered only possible structures having the pyrrole ring and the carbonyl group in a coplanar *cis* arrangement and



BZP: $R = \text{H}$
 CLBZP: $R = \text{Cl}$
 MEBZP: $R = \text{OMe}$

Fig. 1. The title compounds.

concluded that the phenyl ring is rotated by $55 \pm 10^\circ$ from this plane.*

Because of our interest in 2-arylpyrroles (White & McGillivray, 1977) and the uncertainty associated with the above results we have carried out structure analyses of the title compounds. Little work has been done on the structures of simple pyrrolic systems containing a 2-carbonyl substituent, studies being limited to 2-ethoxycarbonylpyrroles containing other ring substituents (Bonnet, Hursthouse & Neidle, 1972) and more complex systems [Cullen, Meyer, Eivazi & Smith (1978), and references quoted therein].

Experimental and structure determination

The preparation of the compounds is described elsewhere (White & McGillivray, 1977). The space groups of BZP and MEBZP were determined photographically. Cell parameters were based on the accurate settings of 25 reflections which were part of data sets collected on a Philips PW 1100 automated four-circle diffractometer. Graphite-monochromated

* In a later paper (Cheng, John, Ritchie, Gore & Farnell, 1975) this figure is quoted as being $70 \pm 10^\circ$.

Table 1. Crystal data and experimental and refinement parameters for BZP, CLBZP and MEBZP

	BZP	CLBZP	MEBZP
Crystal data			
Formula	$\text{C}_{11}\text{H}_9\text{NO}$	$\text{C}_{11}\text{H}_8\text{ClNO}$	$\text{C}_{12}\text{H}_{11}\text{NO}_2$
M_r	171.19	205.63	201.22
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	$P1$	$P2_1/n$	$P2_1/c$
a (Å)	10.687 (5)	11.760 (5)	11.784 (5)
b (Å)	10.623 (5)	21.077 (5)	14.394 (5)
c (Å)	3.953 (5)	3.919 (5)	6.083 (5)
α (°)	98.35 (1)		
β (°)	98.38 (1)	98.08 (1)	102.74 (1)
γ (°)	98.11 (1)		
V (Å ³)	433.2	961.73	1006.37
Z	2	4	4
D_c (Mg m ⁻³)	1.312	1.420	1.328
D_m (Mg m ⁻³)		1.42	
$F(000)$	180	424	424
μ (Mo $K\alpha$) (mm ⁻¹)	0.048	0.308	0.053
Data collection			
Crystal size (mm)	0.1 × 0.4 × 0.3	0.15 × 0.15 × 0.3	0.7 × 0.15 × 0.25
Scan speed (°θ s ⁻¹)	0.04	0.03	0.04
Scan width (°θ)	1.2	0.9	1.2
2θ range (°)	7.5 < 2θ < 46	6.8 < 2θ < 46	6.6 < 2θ < 46
N (reflections)	1203	1256	1473
Number of independent reflections with $I > \sigma(I)$	1177	1091	1369
Final refinement			
R	0.054	0.049	0.081
R_w	0.056	0.066	0.113
k	0.464	1.0	0.278
g	0.0024	0.330	0.0637
U values (Å ²)			
Pyrrole H	0.073 (4)	0.068 (5)	0.064 (7)
Phenyl H	0.080 (4)	0.043 (4)	0.054 (6)
Methyl H			0.088 (10)

Table 2. Fractional atomic coordinates (with e.s.d.'s) ($\times 10^4$) of the non-hydrogen atoms

	BZP			CLBZP			MEBZP		
	x	y	z	x	y	z	x	y	z
N	3384 (2)	-824 (2)	6738 (5)	1182 (2)	5598 (1)	3108 (7)	5375 (3)	799 (2)	12145 (5)
C(1)	2606 (2)	-1867 (2)	7305 (6)	1515 (3)	6175 (2)	2284 (9)	6069 (4)	1149 (3)	10834 (7)
C(2)	1574 (2)	-1462 (2)	8602 (6)	2542 (3)	6131 (2)	1057 (9)	5398 (4)	1696 (3)	9180 (7)
C(3)	1732 (2)	-124 (2)	8821 (6)	2844 (2)	5496 (2)	1141 (8)	4265 (4)	1667 (3)	9489 (6)
C(4)	2865 (2)	266 (2)	7630 (5)	1992 (2)	5164 (1)	2462 (7)	4251 (3)	1104 (3)	11329 (6)
C(5)	3533 (2)	1524 (2)	7408 (5)	1792 (2)	4499 (1)	3030 (7)	3340 (3)	871 (3)	12505 (6)
O(1)	4608 (1)	1668 (1)	6584 (5)	906 (1)	4303 (1)	3998 (7)	3566 (2)	516 (2)	14406 (4)
C(6)	2917 (2)	2681 (2)	8249 (5)	2690 (2)	4022 (1)	2365 (7)	2111 (3)	1071 (3)	11387 (6)
C(7)	1648 (2)	2706 (2)	6932 (6)	3862 (2)	4112 (2)	3373 (8)	1649 (3)	883 (3)	9103 (6)
C(8)	1133 (2)	3824 (2)	7615 (6)	4647 (2)	3659 (1)	2728 (7)	484 (3)	1011 (3)	8160 (7)
C(9)	1872 (3)	4909 (2)	9691 (7)	4255 (2)	3115 (1)	1034 (7)	-243 (3)	1329 (3)	9482 (7)
C(10)	3135 (3)	4887 (2)	11047 (7)	3098 (2)	3001 (1)	53 (8)	198 (4)	1534 (3)	11753 (7)
C(11)	3663 (2)	3781 (2)	10311 (6)	2315 (2)	3455 (1)	752 (8)	1355 (4)	1386 (3)	12697 (6)
Cl				5241 (1)	2546 (0)	52 (3)			
O(2)							-1416 (2)	1492 (2)	8729 (5)
C(12)							-1916 (4)	1357 (4)	6386 (7)

Mo $K\alpha$ ($\lambda = 0.7107 \text{ \AA}$) radiation was used, with an ω - 2θ scan mode. No crystal decomposition was observed. Crystal data and data-collection details are summarized in Table 1.

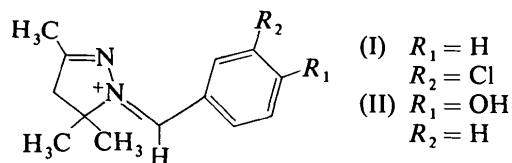
Direct methods were used to locate the atoms, whose positional and thermal parameters were refined by least-squares cycles (Sheldrick, 1976). Convergence was considered complete when no shift/error ratio exceeded 1.0. Final difference maps showed no peak $>0.25 \text{ e \AA}^{-3}$. A weighting scheme $w = k/(\sigma^2 F + gF^2)$ was used, g being refined to give the smallest variation of $w\Delta^2$ with $|F_o|$. The final values of k and g , and the final R values are set out in Table 1. H atoms were positioned geometrically and their thermal parameters refined according to their particular environments. The refined values are given in Table 1. Scattering factors were from Cromer & Mann (1968). Final positional parameters are given in Table 2.* Fig. 2(a) depicts the three molecules, with atomic nomenclature and bond lengths; Fig. 2(b) gives the bond angles. Fig. 3 shows the packing in the unit cells, with the hydrogen bonds represented by thin lines. The intermolecular N—O distances are 2.855 Å in BZP, 2.853 Å in CLBZP and 2.896 Å in MEBZP. Table 3 gives the equations of, and deviations from, relevant least-squares planes, together with the angles between them.

Results and discussion

The structures of the three title compounds substantiate the results of the workers previously cited, namely that

* Lists of structure factors, anisotropic thermal parameters and H-atom positions for the three compounds have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35083 (26 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

in this class of aroylpyrroles the carbonyl group and pyrrole ring form a *cis*-coplanar conjugated system, with the phenyl ring twisted by some 45 – 52° out of the plane. The degree of twist apparently arises as a consequence of steric interaction between the H atoms bound to C(3) and C(7): in all three structures the distance between these atoms is of the order of 2.5 Å . Interestingly, calculations based on the results of Galloway, Nassimbeni & Stephen (1979) show that the phenyl rings in the cations (I) and (II) are twisted out of the plane of the pyrazolinium system by only 21.1 and 13.2° respectively; in this instance there is no steric hindrance to the phenyl ring's being coplanar with the imidazolinium system and the twist is probably due to packing influences. A certain amount of electron delocalization over the entire conjugated system can be inferred in these compounds.



Before considering the differences in bond lengths in the compounds, we note that whereas calculated e.s.d.'s in the bond lengths and angles are some 0.004 Å and 0.3° respectively, it is the general feeling among crystallographers that these figures are underestimated by a factor of at least two (see, for example, Shoemaker, 1974). We therefore regard only bond-length and angle differences of 0.01 Å and 0.8° respectively as significant in the following discussion.

In the pyrrole ring, $\text{N}-\text{C}(1) < \text{N}-\text{C}(4)$ in all three structures, the asymmetry being most marked in CLBZP (0.04 Å). This behaviour has been observed by Bonnet, Hursthouse & Neidle (1972) and Cullen,

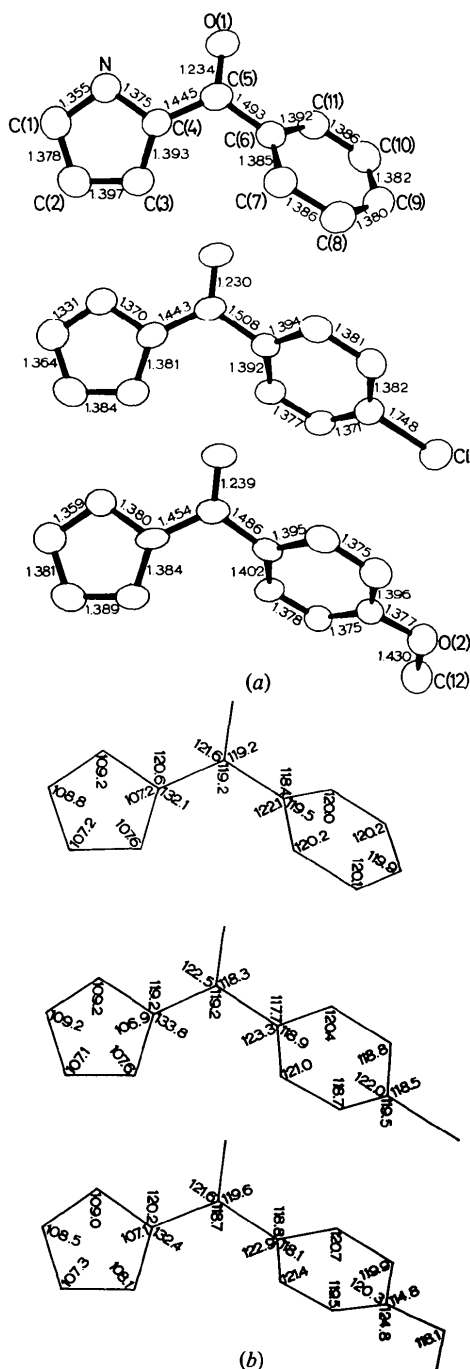


Fig. 2. (a) The structure, atomic nomenclature and bond lengths (Å) for BZP (top), CLBZP (middle) and MEBZP (bottom). Mean bond-length e.s.d.'s are 0.004 Å. (b) Bond angles (°) in the three structures. The order and orientation of the diagram are the same as in (a). Mean e.s.d.'s are 0.3°.

Meyer, Eivazi & Smith (1978) and it appears that these two bonds are the most sensitive to substitution at the α position – in this case at C(4). C(2)–C(3) and C(3)–C(4) show more single-bond character than the

Table 3. *Least-squares planes*

Equations of the planes are expressed in orthogonalized space as $lx + my + nz = P$ and the perpendicular distances (Å) of selected atoms to the plane are given. E.s.d.'s in the atom–plane distances lie in the range 0.001–0.003, 0.001–0.005 and 0.001–0.005 Å for BZP, CLBZP and MEBZP respectively. Atoms marked with an asterisk were not included in the calculation.

BZP

Plane 1: pyrrole ring

$$3.8787x - 0.9981y + 3.4071z = 3.6876$$

N	0.003
C(1)	-0.002
C(2)	0.000
C(3)	0.002
C(4)	-0.003
C(5)*	0.055
O(1)*	0.178
C(6)*	-0.013

Plane 2: phenyl ring

$$-3.9439x - 4.1953y + 3.6428z = 0.7311$$

C(5)*	-0.066
C(6)	-0.001
C(7)	0.009
C(8)	-0.009
C(9)	0.001
C(10)	0.007
C(11)	-0.006

Angle between plane 1 and plane 2: 50.1 (6)°

CLBZP

Plane 1: pyrrole ring

$$4.1786x + 2.5334y + 3.4010z = 2.9730$$

N	-0.004
C(1)	0.001
C(2)	0.002
C(3)	-0.004
C(4)	0.005
C(5)*	-0.054
O(1)*	-0.145
C(6)*	-0.026

Plane 2: phenyl ring

$$-2.2129x - 9.0206y + 3.5336z = -3.3747$$

C(5)*	-0.010
C(6)	-0.013
C(7)	0.003
C(8)	0.010
C(9)	-0.012
C(10)	0.001
C(11)	0.012
C1*	-0.063

Angle between plane 1 and plane 2: 45.5 (1.0)°

MEBZP

Plane 1: pyrrole ring

$$0.6636x + 11.48y + 3.4879z = 5.5053$$

N	0.005
C(1)	-0.005
C(2)	0.002
C(3)	0.001
C(4)	-0.004
C(5)*	0.078
O(1)*	0.348
C(6)*	-0.164

Plane 2: phenyl ring

$$2.9361x + 13.5437y - 1.6948z = 0.1346$$

C(5)*	-0.094
C(6)	0.006
C(7)	0.003
C(8)	-0.006
C(9)	0.013
C(10)	-0.009
C(11)	-0.012
O(2)*	-0.010
C(12)*	0.059

Angle between plane 1 and plane 2: 51.2 (1.1)°

other pyrrole-ring bonds in BZP and CLBZP; however, this distinction is lost in MEBZP. These observations are somewhat at variance with the normal formalization of pyrrole as (III) and a substantial perturbation of the pyrrole ring system by the carbonyl group is apparent. A contribution from the canonical form (IV) may be argued: evidence for participation of the latter may be seen in the considerable shortening of C(4)–C(5) compared with C(5)–C(6). These findings

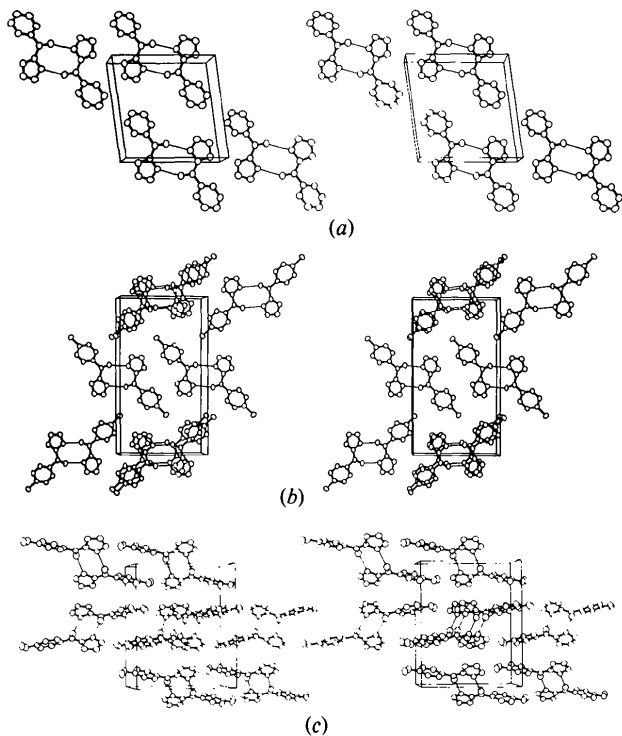
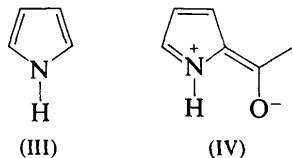


Fig. 3. Packing diagrams for (a) BZP, (b) CLBZP and (c) MEBZP. The projection in each case is on to (001).

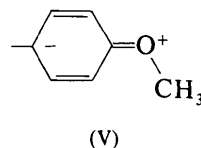
are concomitant with the observation that the carbonyl group in all three structures is very nearly coplanar with the pyrrole ring, suggesting extensive π -electron delocalization. The twist of the phenyl ring renders overlap of its π system with the pyrrole-carbonyl π system minimal in these compounds.



It is interesting to note the contraction of the pyrrole ring caused by the substitution of Cl for H at C(9). This contraction, which amounts on average to 0.014 Å, is greatest in the bonds furthest from the link atom C(4). As pointed out before, π interaction between the phenyl ring and the pyrrole carbonyl system is minimal, and so this effect must be ascribed to the withdrawal of electrons from the pyrrole ring *via* C(5) by the inductive effect. Further support for this is gained from the longer C(5)–C(6) bond in CLBZP.

In view of the structural stability of the phenyl ring, the perturbation in bond lengths resulting from substitution at the *para* positions is noteworthy. While these changes are not insignificant in the case of CLBZP, they are most marked in MEBZP. In this

compound a contribution from (V) may be observed in the lengthening of C(6)–C(11), C(6)–C(7) and C(8)–C(9) [but, curiously, not C(10)–C(9)]. In addition, C(9)–O(2) certainly possesses some double-bond character and the angle subtended at O(2) is close to the ideal sp^2 value of 120° . An instance of this effect, in *p*-methoxybenzoic acid, has been reported by Bryan (1967) who also observes that only the ring bond *trans* to the O–C(methyl) bond is lengthened.



Hydrogen bonds between the pyrrole N and carbonyl O hold the molecules together to form centrosymmetric dimers in all three crystal structures. This pairing is not preserved in benzene solution – the molecular weight of BZP was measured by osmometry to be 170 – reflecting the weakness of the N–H...O bond.

Conclusions

From X-ray crystallographic data it has been possible to confirm the assumption (Cheng, John, Ritchie & Gore, 1974) that in 2-arylpyrroles the pyrrole ring and the carbonyl group are essentially coplanar and that the carbonyl group adopts a *cis* conformation. The plane of the benzene ring in these compounds forms an angle of $45\text{--}52^\circ$ with the plane of the pyrrole ring. This angle is essentially independent of the nature of the substituents in the *para* position of the benzene ring, showing that there is very little, if any, overlap between the π system of the benzene ring and that of the carbonyl group and the pyrrole ring.

Only evidence of intermolecular hydrogen bonding could be found and hence the *cis* conformation cannot be ascribed to intramolecular hydrogen bonding between the pyrrole N–H and the carbonyl O atom.

All calculations were carried out on a Burroughs B6800 computer at the University of South Africa.

The molecular-weight determination was performed by G. Reuter, Alfred Bernhardt Analytical Laboratories, Fritz-Preglstrasse 24, 5270 Gummersbach 1 Elbach, Federal Republic of Germany.

Financial assistance from the University of South Africa (Research Grants Committee) and the CSIR (Pretoria) is gratefully acknowledged. We also thank the CSIR for the diffractometer data collection.

References

- BERTIN, D. M., GARBAY-JAUREGUIBERRY, C., LIEGEOIS, C. & LUMBROSO, H. (1976). *Bull. Soc. Chim. Fr.* pp. 1393–1398.

- BONNET, R., HURSTHOUSE, M. B. & NEIDLE, S. (1972). *J. Chem. Soc. Perkin Trans. 2*, pp. 1335–1340.
- BRYAN, R. F. (1967). *J. Chem. Soc. B*, pp. 1311–1316.
- CHENG, C. H., JOHN, I. G., RITCHIE, G. L. D. & GORE, P. H. (1974). *J. Chem. Soc. Perkin Trans. 2*, pp. 1318–1320.
- CHENG, C. H., JOHN, I. G., RITCHIE, G. L. D., GORE, P. H. & FARNELL, L. (1975). *J. Chem. Soc. Perkin Trans. 2*, pp. 744–751.
- CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst. A* **24**, 321–324.
- CULLEN, D. L., MEYER, E. F., EIVAZI, F. & SMITH, K. M. (1978). *J. Chem. Soc. Perkin Trans. 2*, pp. 259–263.
- GALLOWAY, R. C., NASSIMBENI, L. R. & STEPHEN, A. M. (1979). *Acta Cryst. B* **35**, 1766–1769.
- JOHN, I. G., RITCHIE, G. L. D. & RADOM, L. (1977). *J. Chem. Soc. Perkin Trans. 2*, pp. 1601–1607.
- KAHN, M. K. A. & MORGAN, K. J. (1964). *J. Chem. Soc.* pp. 2579–2585.
- SHELDRIK, G. M. (1976). *SHELX 76*. Program for crystal structure determination. Univ. of Cambridge, England.
- SHOEMAKER, D. P. (1974). *Conference on Critical Evaluation of Chemical and Physical Structure Information*, pp. 157–185. Washington: National Academy of Sciences.
- WHITE, J. & MCGILLIVRAY, G. (1977). *J. Org. Chem.* **42**, 4248–4251.

Acta Cryst. (1980). **B36**, 1141–1146

Structural Studies of Substituted 6,7-Benzomorphan Compounds.

IV. (\pm)-5-Ethyl-2'-hydroxy-9,9-dimethyl-2-phenethyl-6,7-benzomorphan Hydrobromide (Dimephen) and (\pm)-2'-Hydroxy-5,9-dimethyl-2-phenethyl-6,7-benzomorphan (Phenazocine) Hydrobromide Hemihydrate

BY Y. G. GELDERS AND C. J. DE RANTER*

*Laboratorium voor Analytische Chemie en Medicinale Fysicochemie,
Instituut voor Farmaceutische Wetenschappen, KU Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium*

AND M. KOKKES

*Laboratorium voor Kristallografie, Universiteit van Amsterdam, Nieuwe Achtergracht 166, Amsterdam,
The Netherlands*

(Received 22 September 1979; accepted 1 January 1980)

Abstract

Dimephen, $C_{24}H_{32}NO^+.Br^-$, crystallizes in the monoclinic space group $P2_1/c$ with $a = 11.472$ (1), $b = 16.933$ (1), $c = 11.793$ (1) Å, $\beta = 113.019$ (9)° and $Z = 4$. The structure was solved from a Patterson synthesis and refined to $R = 0.046$ for 1993 independent reflections. Phenazocine hydrobromide hemihydrate, $C_{22}H_{28}NO^+.Br^-.1/2H_2O$, has triclinic symmetry, $P\bar{1}$, with $a = 10.263$ (1), $b = 14.307$ (1), $c = 15.835$ (2) Å, $\alpha = 72.506$ (8), $\beta = 72.976$ (8), $\gamma = 69.020$ (6)° and $Z = 4$. A Patterson synthesis revealed the structure which was refined to $R = 0.041$ for 4480 independent reflections. Hydrogen bonds between Br, O and N atoms link the molecules in the crystals of both compounds. The structural data, confirmed by potential-energy calculations, indicate that the conformation of the phenethyl substituent is not critical for the narcotic activity of the compounds considered.

* To whom correspondence should be addressed.

Introduction

(\pm)-5-Ethyl-2'-hydroxy-9,9-dimethyl-2-phenethyl-6,7-benzomorphan hydrobromide, hereafter abbreviated as dimephen,[†] and (\pm)-2'-hydroxy-5,9-dimethyl-2-phenethyl-6,7-benzomorphan hydrobromide hemihydrate, further referred to by its generic name phenazocine,[‡] are both opiate narcotics showing increased analgesic activities of respectively 20 \ddagger and 10 times that of morphine (Janssen & Van der Eycken, 1968). As the benzomorphan skeleton remains essentially unchanged (Gelders & De Ranter, 1980, and preceding papers in this series), the analgesic activity is largely determined by the nature of the substituents. Animal studies have shown that phenethyl substitution on the nitrogen

[†] *Chemical Abstracts* name for dimephen: (\pm)-6-ethyl-1,2,3,4,5,6-hexahydro-2,6-methano-11,11-dimethyl-3-phenethyl-3-benzazocin-8-ol hydrobromide; for phenazocine: 1,2,3,4,5,6-hexahydro-2,6-methano-6,11-dimethyl-3-phenethyl-3-benzazocin-8-ol.

[‡] Private communication from ACF Chemiefarma NV.