drug anions and diethylammonium cations (Fig. 2) with the N4···H1N7 distance equal to 1·81 Å and the N4···H1N7—N7 bond angle equal to 168·5°.

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Structure of 3-(1-Methylethoxy)-7-phenyl-N-(1H-tetrazol-5-yl)-2-benzofurancarboxamide, a Potential Anti-Allergy Agent

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Abstract. $C_{19}H_{17}N_5O_3$, $M_r = 363 \cdot 38$, monoclinic, $P2_1/n$, $a = 7 \cdot 243$ (6), $b = 11 \cdot 452$ (4), $c = 20 \cdot 552$ (4) Å, $\beta = 93 \cdot 93$ (3)°, $V = 1701$ (2) Å^3, $Z = 4$, $D_x = 1 \cdot 419$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, $\mu = 0 \cdot 093$ mm^{-1}, $F(000) = 760$, $T = 293$ K, final $R = 0 \cdot 027$ for 1239 observed reflections with $I > 3\sigma(I)$. The benzofuran moiety is essentially planar with the phenyl ring inclined at 139·53 (7)° to it. The tetrazole ring is also planar with the mean planes of the tetrazole ring and the benzofuran moiety lying at 8·1 (2)°. The carboxamide chain is fully extended with a CC—NC torsion angle of 177·7 (2)°. H atoms on the N atoms are involved in short intramolecular contacts (O···H 2·058 and 2·236 Å).

Introduction. We have reported the crystal structure of 5-methoxy-3-(1-methylethoxy)-1-phenyl-N-(1H-tetrazol-5-yl)-1H-indole-2-carboxamide–diethylamine (1) (Parvez, Unangst, Connor & Mullican, 1991). Compound (1) is a potent inhibitor of allergic mediator release from human basophils and from guinea pig and human chopped lung tissue challenged with anti-IgE (Unangst, Connor, Stabler, Weikert, Carethers, Kennedy, Thueson, Chestnut, Adolphson & Conroy, 1989). The crystal structure of

(2), a benzofuran analogue of (1), was determined to assist molecular-modeling studies in understanding the structural and conformational features necessary for inhibition of allergic mediator release.

(1)   (2)
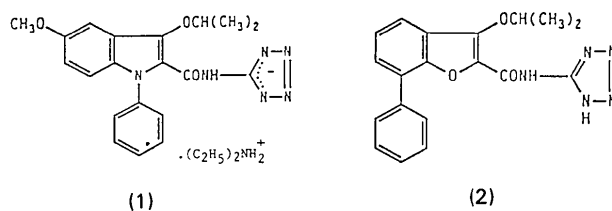
Experimental. A mixture of 8·8 g (0·030 mol) of 3-(1-methylethoxy)-7-phenyl-2-benzofurancarboxylic acid (Connor, Cetenko, Unangst & Johnson, 1987) and 5·5 g (0·034 mol) of 1,1'-carbonylbis(1H-imidazole) in 180 ml of acetonitrile was stirred at reflux under a nitrogen atmosphere for 90 min. The cooled reaction mixture was treated with 3·0 g (0·035 mol) of anhydrous 5-aminotetrazole, followed by 10·0 ml (7·3 g; 0·072 mol) of triethylamine. The mixture was again stirred at reflux for 16 h, cooled, added to 750 g of ice and water, and acidified with acetic acid. The precipitated product was filtered, washed with water, and recrystallized from methanol/N,N-

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Table 1. Summary of data collection and structure refinement

Crystal size (mm)	0·15 × 0·20 × 0·45
Diffractometer	Enraf–Nonius CAD-4
Monochromator	Graphite
Cell constants	25 reflections, 10 < θ < 15°
θ$_{max}$ (°)	20
Scan method	ω/2θ
ω-scan width (°)	0·70 + 0·35tanθ
Variable scan speed (° min^{-1})	0·55–3·3
Scan ranges of h, k, l	0→7, 0→11, −20→20
Intervals of standard reflections (s)	3600
Crystal decay	Insignificant
Data correction applied*	Lorentz and polarization
Unique data measured	1567
Data used [I > 3σ(I)]	1239
R$_{int}$	0·007
Parameters refined	244
R, wR	0·027, 0·033
Weighting scheme	$w = [\sigma^2(F_o) + (0.040F_o)^2]^{-1}$
(Δ/σ)$_{max}$ in last cycle	<0·01
Δρ$_{min,max}$ in final ΔF map (e Å^{-3})	−0·23, 0·12
S	1·348

* Absorption ignored.

dimethylformamide/water to yield 7·8 g (72% yield) of tetrazole product, after washing with hexane; m.p. 497 K dec.

Details of data collection and structure refinement are given in Table 1. The structure was solved by direct methods (*MULTAN*11/82; Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982) and refined by full-matrix least-squares calculations on *F*'s. H atoms were located from a difference map and included at these positions in the structure-factor calculations with the overall isotropic temperature factor $B_{iso} = 4·0$ Å^2; C, N and O had anisotropic temperature factors. Scattering factors used in the calculations were taken from Cromer & Mann (1968) and Stewart, Davidson & Simpson (1965). Computer programs used in this study were from the Enraf–Nonius *Structure Determination Package* (B. A. Frenz & Associates, Inc., 1985) and *ORTEP*II (Johnson, 1976).

Discussion. Final fractional coordinates and equivalent isotropic thermal parameters with e.s.d.'s are listed in Table 2.* Table 3 contains bond lengths and angles. Fig. 1 shows the molecular structure of the title compound. Fig. 2 is a stereoview of the unit-cell packing. The benzofuran moiety is essentially planar with maximum deviation of any atom 0·008 (2) Å. The phenyl ring is also planar [max. deviation 0·001 (2) Å] and is inclined at 139·53 (7)° to the benzofuran moiety. The tetrazole ring is planar to

* Lists of structure factors, anisotropic thermal parameters, least-squares-planes data and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53307 (19 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Final fractional coordinates and equivalent isotropic thermal parameters (Å²) with e.s.d.'s in parentheses

$$B_{eq} = a^2B_{11} + b^2B_{22} + c^2B_{33} + ab\cos\gamma B_{12} + ac\cos\beta B_{13} + bc\cos\alpha B_{23}.$$

	x	y	z	B$_{eq}$
O(1)	0·2200 (2)	0·0151 (1)	0·43063 (5)	2·95 (3)
O(2)	0·3296 (2)	0·0309 (1)	0·60052 (6)	3·61 (3)
O(3)	0·1481 (2)	−0·2141 (1)	0·45432 (6)	3·90 (3)
N(1)	0·2234 (2)	−0·1943 (1)	0·56231 (7)	3·05 (4)
N(2)	0·2188 (3)	−0·3531 (2)	0·63650 (8)	4·08 (4)
N(3)	0·1584 (3)	−0·4654 (2)	0·63060 (8)	4·50 (4)
N(4)	0·0924 (2)	−0·4870 (2)	0·57222 (8)	4·07 (4)
N(5)	0·1108 (2)	−0·3869 (1)	0·53858 (7)	3·40 (4)
C(1)	0·2633 (3)	0·1310 (2)	0·43575 (9)	2·69 (4)
C(2)	0·2610 (3)	0·2069 (2)	0·38273 (9)	2·84 (4)
C(3)	0·3106 (3)	0·3200 (2)	0·39862 (9)	3·55 (5)
C(4)	0·3583 (3)	0·3554 (2)	0·4623 (1)	3·82 (5)
C(5)	0·3596 (3)	0·2789 (2)	0·51332 (9)	3·58 (5)
C(6)	0·3117 (3)	0·1624 (2)	0·50023 (8)	2·76 (4)
C(7)	0·2960 (3)	0·0558 (2)	0·53677 (9)	2·79 (4)
C(8)	0·2402 (2)	−0·0290 (2)	0·49343 (8)	2·67 (4)
C(9)	0·2137 (3)	0·1709 (2)	0·31464 (9)	2·91 (4)
C(10)	0·3138 (3)	0·2146 (2)	0·2648 (1)	3·85 (5)
C(11)	0·2721 (3)	0·1824 (2)	0·2012 (1)	4·36 (5)
C(12)	0·1305 (3)	0·1065 (2)	0·18598 (9)	4·09 (5)
C(13)	0·0293 (3)	0·0624 (2)	0·2344 (1)	4·02 (5)
C(14)	0·0706 (3)	0·0941 (2)	0·29826 (9)	3·42 (5)
C(15)	0·3792 (3)	0·1240 (2)	0·64729 (9)	3·12 (4)
C(16)	0·4618 (3)	0·0636 (2)	0·7067 (1)	4·28 (5)
C(17)	0·2120 (3)	0·1939 (2)	0·6603 (1)	4·15 (5)
C(18)	0·1999 (3)	−0·1515 (2)	0·49973 (8)	2·75 (4)
C(19)	0·1861 (3)	−0·3073 (2)	0·57856 (9)	2·85 (4)

Table 3. Bond distances (Å) and bond angles (°)

O(1)	C(1)	1·367 (2)		C(2)	C(9)	1·476 (2)		
O(1)	C(8)	1·384 (2)		C(3)	C(4)	1·391 (3)		
O(2)	C(7)	1·347 (2)		C(4)	C(5)	1·367 (3)		
O(2)	C(15)	1·464 (2)		C(5)	C(6)	1·400 (2)		
O(3)	C(18)	1·216 (2)		C(6)	C(7)	1·442 (2)		
N(1)	C(18)	1·376 (2)		C(7)	C(8)	1·361 (2)		
N(1)	C(19)	1·367 (2)		C(8)	C(18)	1·440 (2)		
N(2)	N(3)	1·361 (2)		C(9)	C(10)	1·388 (3)		
N(2)	C(19)	1·308 (2)		C(9)	C(14)	1·383 (3)		
N(3)	N(4)	1·285 (2)		C(10)	C(11)	1·372 (3)		
N(4)	N(5)	1·349 (2)		C(11)	C(12)	1·365 (3)		
N(5)	C(19)	1·320 (2)		C(12)	C(13)	1·372 (3)		
C(1)	C(2)	1·393 (2)		C(13)	C(14)	1·374 (3)		
C(1)	C(6)	1·394 (2)		C(15)	C(16)	1·492 (3)		
C(2)	C(3)	1·377 (2)		C(15)	C(17)	1·491 (3)		
C(1)	O(1)	C(8)	105·9 (1)		C(6)	C(7)	C(8)	107·1 (2)
C(7)	O(2)	C(15)	120·3 (1)		O(1)	C(8)	C(7)	110·9 (2)
C(18)	N(1)	C(19)	123·5 (2)		O(1)	C(8)	C(18)	115·5 (2)
N(3)	N(2)	C(19)	105·1 (2)		C(7)	C(8)	C(18)	133·6 (2)
N(2)	N(3)	N(4)	111·2 (2)		C(2)	C(9)	C(10)	119·9 (2)
N(3)	N(4)	N(5)	105·8 (1)		C(2)	C(9)	C(14)	122·0 (2)
N(4)	N(5)	C(19)	108·6 (1)		C(10)	C(9)	C(14)	118·1 (2)
O(1)	C(1)	C(2)	123·7 (2)		C(9)	C(10)	C(11)	120·9 (2)
O(1)	C(1)	C(6)	111·4 (2)		C(10)	C(11)	C(12)	120·2 (2)
C(2)	C(1)	C(6)	124·9 (2)		C(11)	C(12)	C(13)	119·9 (2)
C(1)	C(2)	C(3)	114·3 (2)		C(12)	C(13)	C(14)	120·3 (2)
C(1)	C(2)	C(9)	123·8 (2)		C(9)	C(14)	C(13)	120·7 (2)
C(3)	C(2)	C(9)	121·8 (2)		O(2)	C(15)	C(16)	105·4 (1)
C(2)	C(3)	C(4)	122·8 (2)		O(2)	C(15)	C(17)	110·1 (2)
C(3)	C(4)	C(5)	121·5 (2)		C(16)	C(15)	C(17)	112·8 (2)
C(4)	C(5)	C(6)	118·4 (2)		O(3)	C(18)	N(1)	121·3 (2)
C(1)	C(6)	C(5)	118·1 (2)		O(3)	C(18)	C(8)	124·0 (2)
C(1)	C(6)	C(7)	104·7 (2)		N(1)	C(18)	C(8)	114·7 (2)
C(5)	C(6)	C(7)	137·2 (2)		N(1)	C(19)	N(2)	125·1 (2)
O(2)	C(7)	C(6)	132·1 (2)		N(1)	C(19)	N(5)	125·6 (2)
O(2)	C(7)	C(8)	120·7 (2)		N(2)	C(19)	N(5)	109·3 (2)
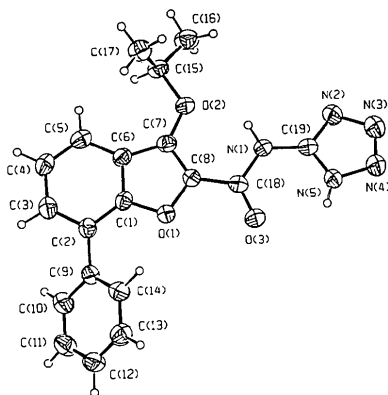
Fig. 1. *ORTEP* drawing of the title compound showing numbering scheme.

The corresponding torsion and mean-planes angles in (1) were 174·9 (3) and 10·8 (4)°, respectively (Parvez, Unangst, Connor & Mullican, 1991).

The bond distances and angles in the benzofuran moiety and its substituents, phenyl, methylethoxy, and carboxamide groups, are unexceptional. In the tetrazole ring, the N(3)—N(4) distance [1·285 (2) Å] is clearly indicative of a double bond, which is significantly shorter than N(2)—N(3) and N(4)—N(5) single bonds [1·361 (2) and 1·349 (2) Å, respectively]. There are no unusual intermolecular distances less than van der Waals contacts. However, H atoms on the N(1) and N(5) atoms are directed towards O(2) and O(3), respectively, resulting in intramolecular contacts of 2·058 and 2·236 Å, respectively.

Fig. 2. Stereoview of a unit cell showing molecular packing.

within 0·004 (2) Å and is linked to the benzofuran moiety through a fully extended carboxamide group which exhibits a C(8)C(18)—N(1)C(19) torsion angle of 177·7 (2)°. The mean planes of the benzofuran moiety and the tetrazole ring are oriented at 8·1 (2)°.

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Structure and Absolute Configuration of an Antihistaminic Drug, Clemastine Hydrogen Fumarate

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Abstract. 2-{2-[1-(4-Chlorophenyl)-1-phenylethoxy]-ethyl}-1-methylpyrrolidinium hydrogen fumarate, $C_{21}H_{27}ClNO^+.C_4H_3O_4^-$, $M_r = 459·97$, orthorhombic, $P2_12_12_1$, $a = 9·414$ (2), $b = 13·154$ (1), $c = 19·535$ (2) Å, $V = 2419·1$ Å^3, $Z = 4$, $D_x = 1·263$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 1·684$ mm^{-1}, $F(000) = 976$, $T = 293$ (1) K, $R = 0·0564$ for 2130 observed reflections with $I > 3\sigma(I)$. Both six-membered rings are individually planar with their mean planes almost perpendicular to each other [angle 88·0 (1)°]. The pyrrolidine ring exhibits an envelope conformation and is protonated at the N