Reaction of Ketenes with *N,N*-Disubstituted α-Aminomethyleneketones. XIX. Synthesis of *N,N*-Disubstituted 4-Amino-3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones (4-Amino-3-phenylangelicins). Crystal and Molecular Structure of 3-Phenylangelicin

Luisa Mosti, Pietro Schenone* and Giulia Menozzi

Istituto di Scienze Farmaceutiche dell'Università, Viale Benedetto XV-3,
16132 Genova, Italy

Fernando Sancassan

Istituto di Chimica Organica dell'Università, Palazzo delle Scienze, Corso Europa,
16132 Genova, Italy

Francarosa Baccichetti

Istituto di Chimica Farmaceutica dell'Università, Centro di Studio sulla Chimica del Farmaco e dei
Prodotti Biologicamente Attivi del C.N.R.,
35100 Padova, Italy

Franco Benetollo

Istituto di Chimica e Tecnologia dei Radioelementi - C.N.R., Corso Stati Uniti 4,
35100 Padova, Italy

Gabriella Bombieri

Istituto di Chimica Farmaceutica e Tossicologica, Università di Milano, Viale Abruzzi 42,
20131 Milano, Italy

Received July 9, 1987

1,4-Cycloaddition of phenylchloroketene to *N,N*-disubstituted 5-aminomethylene-6,7-dihydrobenzo[*b*]furan-4(5*H*)-ones gave the corresponding adducts, namely *N,N*-disubstituted 4-amino-3-chloro-3,4,5,6-tetrahydro-3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones **II**, which were dehydrochlorinated with DBN to *N,N*-disubstituted 4-amino-5,6-dihydro-3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones **III**. Compounds **III** afforded the title compounds **IV** by dehydrogenation with DDQ. In the cycloaddition step, 3-phenylangelicin **V**, whose structure was confirmed by ^{1}H-nmr shift reagents data and by X-ray crystal structure determination, was almost always formed, probably starting from **II** by dehydrochlorination, dehydrogenation and hydrogenolysis of the disubstituted amino group. Separation of **V** was achieved by alumina chromatography either in the cycloaddition step or, in most cases, in the dehydrochlorination step.

3-Phenylangelicin crystallizes in the trigonal system, space group R$\bar{3}$, with cell parameters (hexagonal axes) a = b = 41.021(10), c = 3.888(2) Å. The angelicin moiety forms a dihedral angle of 42.1(1)° with the phenyl substituent. Disordered solvent molecules of ethyl acetate are clathrated in channels in the direction of the crystallographic axis *c*.

J. Heterocyclic Chem., **25**, 407 (1988).

The dipolar 1,4-cycloaddition of dichloroketene to *N,N*-disubstituted α-aminomethyleneketones, when applied to a series of 5-aminomethylene-6,7-dihydrobenzo-[*b*]furan-4(5*H*)-ones **I**, led us to the synthesis of *N,N*-disubstituted 4-amino-3-chloro-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones (4-amino-3-chloroangelicins), some of which showed an interesting photochemotherapeutic activity as antiproliferative compounds [1,2].

Our recent work on the cycloaddition of *N,N*-disubstituted enaminones to phenylchloroketene [3,4] prompted us to study the reaction of this ketene with enaminones **I**, in order to obtain other potentially active angelicin derivatives, where the chlorine atom of 4-amino-3-chloroangelicins was replaced by the phenyl group.

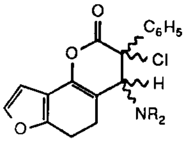
The reaction of phenylchloroketene (prepared *in situ* from 2-chloro-2-phenylacetyl chloride and triethylamine [3]) with enaminones **Ia-g** [1] occurred both in the case of aliphatic and aromatic *N*-substitution to give the cycloadducts **IIa-g**. In the reaction mixture was also present, generally in moderate amounts, 3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-one (3-phenylangelicin) **V**, which was probably formed starting from adducts **II** by dehydrochlorination, dehydrogenation and hydrogenolysis of the disubstituted amino group [5].

This fact could account for the low yield of the primary adducts, at least in those cases where their separation by alumina chromatography and characterization were possible (compounds **IId,f**, Table I). In all other cases, we were unable to separate **V** from **II**, therefore the crude reaction product was employed in the next step.

The structure of 3-phenylangelicin **V**, already obtained by a lengthy route [7], was confirmed by ^{1}H-nmr shift

Table I

N,N-Disubstituted 4-Amino-3-chloro-3,4,5,6-tetrahydro-3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones **IId,f**



Formula Number	NR$_2$	Reaction time (hours)	Yield %	Mp °C [a]	Molecular Formula	Analyses % Calcd./Found C	H	N
IId	1-Piperidinyl	20	28 (33) [b]	124-126	$C_{22}H_{22}ClNO_3$	68.83	5.78	3.65
						68.74	5.92	3.73
IIf	$N(CH_3)C_6H_5$	90	56 (30) [b]	141-142	$C_{24}H_{20}ClNO_3$	71.02	4.97	3.45
						71.03	5.06	3.73

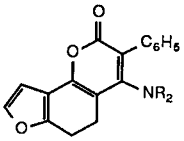
IR and NMR Spectral Data

	IR, cm^{-1} C=O	C=C	NMR, δ
IId	1772	1672	1.51 (mc, 3 CH$_2$ pip), 2.1-3.0 (m, 2 CH$_2$N + CH$_2$-5 + CH$_2$-6), 3.82 (s, CH-4), 6.43 (d, J = 1.8, CH-9), 7.1-7.6 (m, C$_6$H$_5$ + CH-8)
IIf	1775	1678	2.1-2.8 (m, CH$_2$-5 + CH$_2$-6), 2.86 (s, CH$_3$N), 5.07 (s, CH-4), 6.46 (d, J = 1.8, CH-9), 6.6-7.7 (m, 2 C$_6$H$_5$ + CH-8)

[a] From diethyl ether. [b] The value between brackets indicates the yield of **V**.

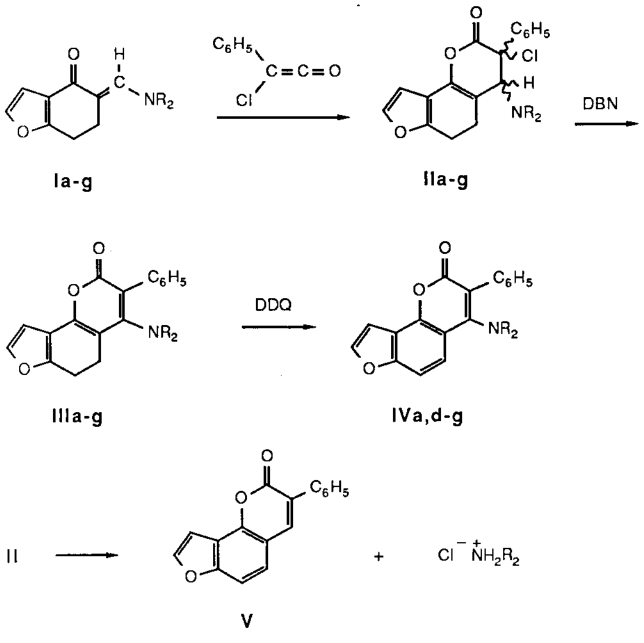
Table II

N,N-Disubstituted 4-Amino-5,6-dihydro-3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones **IIIa-g**



Formula Number	NR$_2$	Yield %	Mp °C [a]	Molecular Formula	Analyses % Calcd./Found C	H	N
IIIa	$N(CH_3)_2$	26 (17) [b]	232-233	$C_{19}H_{17}NO_3$	74.25	5.57	4.56
					74.03	5.64	4.75
IIIb	$N(C_2H_5)_2$	28 (22) [b]	205-207	$C_{21}H_{21}NO_3$	75.20	6.31	4.18
					75.10	6.29	4.20
IIIc	1-Pyrrolidinyl	11 (28) [b]	225-226	$C_{21}H_{19}NO_3$	75.66	5.74	4.20
					75.63	5.75	4.23
IIId	1-Piperidinyl	69	188-190	$C_{22}H_{21}NO_3$	76.06	6.09	4.03
					76.18	5.90	3.84
IIIe	4-Morpholinyl	36 (52) [b]	240-242	$C_{21}H_{19}NO_4$	72.19	5.48	4.01
					72.04	5.60	3.89
IIIf	$N(CH_3)C_6H_5$	79	233-234	$C_{24}H_{19}NO_3$	78.03	5.18	3.79
					77.99	5.18	4.09
IIIg	$N(C_6H_5)_2$	84	222-224	$C_{29}H_{21}NO_3$	80.72	4.90	3.25
					80.42	4.78	3.05

[a] From ethyl acetate. [b] The value between brackets indicates the yield of **V**.



NR_2 : a) $N(CH_3)_2$; b) $N(C_2H_5)_2$; c) 1-Pyrrolidinyl; d) 1-Piperidinyl; e) 4-Morpholinyl; f) $N(CH_3)C_6H_5$; g) $N(C_6H_5)_2$

reagents data (see Experimental) and by X-ray crystal structure determination (see below).

Cycloadducts **IIa-g** were dehydrochlorinated in refluxing toluene with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) to afford *N,N*-disubstituted 4-amino-3-phenyl-5,6-dihydro-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones **IIIa-g** (Table II), the structures of which were confirmed by their uv, ir and nmr spectral data (Table III).

Table III

UV, IR and NMR Spectral Data of Compounds **IIIa-g**

Compound	UV, λ max nm (log ε)	IR, cm^{-1} C=O	IR, cm^{-1} C=C	NMR, δ
IIIa	215 (4.36) 232 sh (4.15) 252 sh (4.10) 265 sh (3.96) 357 (4.23)	1677	1620 1523	2.48 [s, $(CH_3)_2N$], 2.94 (s, CH_2-5 + CH_2-6), 6.73 (d, J = 1.8, CH-9), 7.33 (mc, C_6H_5 + CH-8)
IIIb	228 (3.99) 247 sh (3.95) 265 sh (3.83) 353 (4.19)	1683	1624 1517	1.00 (t, J = 7.2, 2 CH_3), 2.76 (q, J = 7.2, 2 CH_2N), 2.92 (near s, CH_2-5 + CH_2-6), 6.75 (mc, CH-9), 7.36 (mc, C_6H_5 + CH-8)
IIIc	230 (4.29) 243 sh (4.27) 267 sh (4.14) 353 (4.37)	1680	1626 1515	1.66 (mc, 2 CH_2 pyr), 2.95 (mc, 2 CH_2N + CH_2-5 + CH_2-6), 6.75 (d, J = 1.8, CH-9), 7.32 (mc, C_6H_5 + CH-8)
IIId	236 (4.07) 246 sh (4.05) 265 sh (3.86) 353 (4.21)	1677	1617 1516	1.46 (mc, 3 CH_2 pip), 2.59 (mc, 2 CH_2N), 2.94 (s, CH_2-5 + CH_2-6), 6.70 (d, J = 1.8, CH-9), 7.33 (mc, C_6H_5 + CH-8)
IIIe	234 (4.11) 250 sh (4.01) 270 sh (3.81) 362 (4.26)	1688	1623 1524	2.66 (t, J = 4.2, 2 CH_2N), 2.95 (s, CH_2-5 + CH_2-6), 3.60 (t, J = 4.2, 2 CH_2O), 6.73 (d, J = 1.8, CH-9), 7.36 (mc, C_6H_5 + CH-8)
IIIf	212 (4.30) 240.5 (4.17) 255 sh (4.02) 275 sh (3.77) 379 (4.22)	1690	1615 1520	2.4-2.8 (m, CH_2-5 + CH_2-6), 2.73 (s, CH_3N), 6.6-7.1 (m, 4 H ar + CH-9), 7.15-7.55 (m, 6 H ar + CH-8)
IIIg	282 (4.235) 380 (4.25)	1694	1620 1526	2.2-3.0 (m, CH_2-5 + CH_2-6), 6.75 (d, J = 1.8, CH-9), 6.8-7.2 (m, 3 C_6H_5), 7.34 (d, J = 1.8, CH-8)

Yields were good in the case of **IIId,f,g** and moderate in the other cases, **IIIa-c,e**; the latter compounds were separated by alumina chromatography from variable amounts (17-52%) of 3-phenylangelicin **V**.

Finally, compounds **IIIa,d-g** were dehydrogenated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in refluxing toluene to give in excellent yields *N,N*-disubstituted 4-amino-3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones (4-amino-3-phenylangelicins) **IVa,d-g** (Table IV), whose structures were proven by their uv, ir and nmr spectral data (Table V).

Apart from the synthetic results, this cycloaddition allowed, at least in the most favourable case, **IIe**, a facile access to 3-phenylangelicin **V** in three steps and in 41% overall yield starting from 6,7-dihydrobenzo[*b*]furan-4(5*H*)-one [1], whereas the described synthesis of **V** [7] involved still three steps but with a 15% overall yield and starting from a coumarin derivative not easily available.

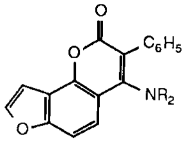
The photobiological properties of compounds **IVa,f** and **V** were evaluated by their capacity to inhibit DNA synthesis in Ehrlich ascites tumor cells and to photoinduce erythema on guinea pig skin as previously described [1]. Unfortunately the scarce solubility of the compounds in the solvent used (normal saline plus 1% v/v ethanol) did not allow to evidence significant inhibition of DNA synthesis, whereas they showed no phototoxicity on guinea pig skin test.

Crystal Structure Determination of 3-Phenylangelicin V.

The final atomic parameters are given in Table VI, bond distances and angles in Table VII. A perspective view of the molecule and the numbering scheme used are shown in Figure 1. The asymmetric unit is constituted by a single molecule. Mean plane calculations through the

Table IV

N,N-Disubstituted 4-Amino-3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones **IVa, d-g**



Formula Number	NR_2	Reaction time (hours)	Yield %	Mp °C	Molecular Formula	Analyses % Calcd./Found C	H	N
IVa	$N(CH_3)_2$	22	71	195-197 [a]	$C_{19}H_{15}NO_3$	74.74 74.61	4.95 4.86	4.59 4.38
IVd	1-Piperidinyl	50	60	220-221 [a]	$C_{22}H_{19}NO_3$	76.50 76.31	5.54 5.60	4.05 3.87
IVe	4-Morpholinyl	48	89	264-265 [a]	$C_{21}H_{17}NO_4$	72.61 72.49	4.93 5.08	4.03 3.95
IVf	$N(CH_3)C_6H_5$	60	94	217-218 [b]	$C_{24}H_{17}NO_3$	78.46 78.61	4.66 4.80	3.81 3.98
IVg	$N(C_6H_5)_2$	48	100	224-226 [a]	$C_{29}H_{19}NO_3$	81.10 81.00	4.46 4.50	3.26 3.10

[a] From 95% ethanol. [b] From ethyl acetate.

Table V

UV, IR and NMR Spectral Data of Compounds **IVa,d-g**

Compound	UV, λ max nm (log ε)	IR, cm^{-1}	NMR, δ
IVa	217 (4.24) 220 (4.235) 242 sh (4.35) 247.5 (4.37) 295 (3.97) 324 (4.055)	1692 1604 1554	2.68 [s, $(CH_3)_2N$], 7.16 (d, J ~2, CH-9), 7.37 (mc, C_6H_5), 7.39 (d, J = 8.4, CH-6), 7.68 (d, J = 8.4, CH-5), 7.73 (d, J ~ 2, CH-8)
IVd	220 (4.34) 240 sh (4.47) 246 (4.48) 300 (4.09) 325 (4.17)	1695 1605 1554	1.57 (mc, 3 CH_2 pip), 2.81 (mc, 2 CH_2N), 7.20 (mc, CH-9), 7.38 (mc, C_6H_5 + CH-5 + CH-6), 7.65 (mc, CH-8)
IVe	217 (4.50) 240 sh (4.58) 246.5 (4.61) 303 (4.26) 322 (4.28)	1697 1605 1556	2.86 (t, J = 4.5, 2 CH_2N), 3.75 (t, J = 4.5, 2 CH_2O), 7.16 (mc, CH-9), 7.2-7.9 (m, C_6H_5 + CH-5 + CH-6 + CH-8)
IVf	217 sh (4.14) 248 (4.23) 265 sh (3.83) 307 (3.82) 314 (3.81) 380 (3.40)	1705 ~1620 1598 1558	2.90 (s, CH_3N), 6.5-7.5 (m, 2 C_6H_5 + CH-5 + CH-6), 6.78 (d, J ~ 2, CH-9), 7.65 (d, J ~ 2, CH-8)
IVg	249 (4.62) 254 sh (4.60) 265 sh (4.44) 284 (4.41) 327 sh (4.18) 385 (3.99)	1710 1628 1603 1563	6.2-7.5 (m, 17 H ar + CH-9), 7.70 (mc, CH-8)

tricyclic moiety show with good approximation planarity of the system (the Δ values range from -0.034(1) to 0.016(2) Å) while the carbonyl oxygen O(2) deviates significantly from this mean plane (Δ = 0.079(2) Å). The phenyl group forms with this system a dihedral angle of 41.7(1)°. The orientation assumed by the phenyl substituent is in order to minimize intramolecular contacts with carbons of the angelicin moiety (In particular C(4)...C(15) is 2.998(4) Å and C(2)...C(19) 3.056(4) Å). However, this causes an internal O...H contact between O(2) and H(19) of 2.61(3) Å while O(2)...C(19) is 2.990(4) Å with a C(19)-H(19)...O(2) angle of 103(2)°. (The value of the angle suggests a weak O...H interaction rather than hydrogen bond). A comparison with the structure of angelicin [8] shows interesting features. Both are characterized by a short *c* cell parameter [3.781(5) Å in angelicin and 3.888(1) Å in compound **V**], this causing in both cases interactions between molecules translated by *c* (packing distances of 3.41 Å in angelicin and 3.44 Å in the tricyclic moiety of compound **V**).

The O(2) in angelicin forms intermolecular contacts with H(5) (2.49 Å) of an adjacent molecule and with H(12) (2.53 Å) of a second adjacent molecule. Here significant intermolecular contacts are between O(1) and H(13)' 2.63(3) Å (' at the position 2/3-x, 1/3-y, -1/3-z); O(2)...H(12)' 2.66(3) Å and O(2)...H(16)'' [2.64(3) Å] ('' at the position y+1/3, 2/3-x+y, -2+2/3-z). Other contacts are O(11)...

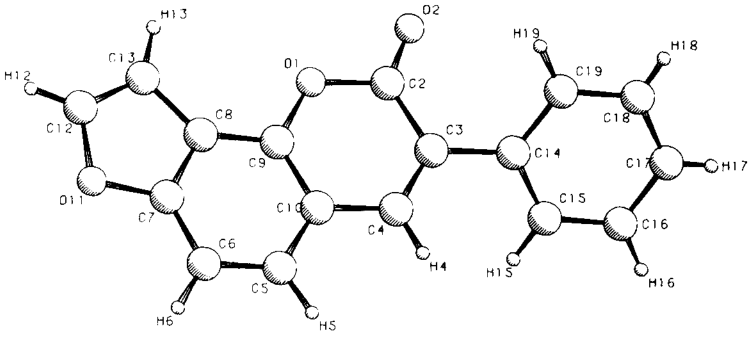


Figure 1. Perspective view of 3-phenylangelicin molecule.

H(4)''' 2.97(2) Å and O(11)...H(5)''' 2.93(3) Å (''' at the position -2/3-y, x-1/3-y, -1/3+z). These are, in any case, longer when compared with the previous ones. In fact in compound **V** the crystal cohesion is reinforced by the additional π interactions between the phenyls which are separated by a *c* parameter (packing distance 3.60 Å) rather than by C-H...O contacts. This means that differently from *N,N*-dimethyl-4-amino-3-chloroangelicin [9] where the substituents at the angelicin moiety hinder a close packing, here the phenyl substituent favours the crystal packing.

Table VI

Atomic Coordinates (x10^4), and U Equivalent**/iso (x10^3) with e.s.d.'s in Parentheses

	a/x	b/y	c/z	Ueq/Uiso*
O1	3905(1)	1599(1)	-2207(4)	45(1)
O2	4390(1)	2074(1)	-4724(6)	69(1)
O11	2824(1)	631(1)	2670(5)	60(1)
C2	4282(1)	1784(1)	-3181(7)	46(1)
C3	4500(1)	1602(1)	-2334(6)	40(1)
C4	4326(1)	1261(1)	-796(6)	42(1)
C5	3750(1)	719(1)	1805(7)	45(1)
C6	3377(1)	551(1)	2715(7)	48(1)
C7	3193(1)	748(1)	1943(7)	46(1)
C8	3359(1)	1098(1)	320(7)	42(1)
C9	3737(1)	1256(1)	-579(6)	39(1)
C10	3936(1)	1073(1)	157(6)	40(1)
C13	3072(1)	1198(1)	28(8)	54(2)
C12	2764(1)	917(1)	1454(10)	66(2)
C14	4904(1)	1794(1)	-3270(6)	40(1)
C15	5057(1)	1587(1)	-4617(7)	50(2)
C16	5436(1)	1755(1)	-5418(8)	60(2)
C17	5666(1)	2134(1)	-4831(8)	61(2)
C18	5520(1)	2344(1)	-3480(8)	57(2)
C19	5140(1)	2178(1)	-2732(7)	46(1)
H4	4466(6)	1136(6)	-212(58)	42(7)*
H5	3904(7)	601(7)	2313(60)	47(7)*
H6	3256(7)	303(7)	3902(61)	48(7)*
H13	3093(8)	1428(8)	-1025(68)	65(9)*
H12	2510(9)	883(9)	1902(79)	88(11)*
H15	4893(8)	1304(8)	-5092(68)	67(9)*
H16	5533(8)	1597(8)	-6417(72)	73(9)*
H17	5937(9)	2267(8)	-5308(73)	73(9)*
H18	5686(8)	2620(8)	-3035(68)	65(9)*
H19	5041(7)	2328(7)	-1684(61)	49(7)*

** Equivalent U defined as one third of the trace of the orthogonalized U_{ij} tensor.

Table VII

Selected Bond Distances (Å) and Angles (°) with e.s.d.'s in Parentheses

Distances

O1-C2	1.393(3)	C7-C8	1.394(4)
O1-C9	1.372(3)	C8-C9	1.392(4)
O2-C2	1.201(4)	C8-C13	1.434(5)
O11-C7	1.372(3)	C9-C10	1.388(5)
O11-C12	1.395(5)	C13-C12	1.330(4)
C2-C3	1.460(5)	C14-C15	1.390(5)
C3-C4	1.349(4)	C14-C19	1.390(4)
C3-C14	1.481(4)	C15-C16	1.382(4)
C4-C10	1.432(4)	C16-C17	1.375(5)
C5-C6	1.374(4)	C17-C18	1.377(6)
C5-C10	1.413(4)	C18-C19	1.385(4)
C6-C7	1.383(5)		
C4-H4	.97(3)	C15-H15	1.02(3)
C6-H6	.99(2)	C16-H16	1.00(4)
C5-H5	.99(3)	C17-H17	1.00(3)
C13-H13	.99(3)	C18-H18	1.001(3)
C12-H12	1.00(4)	C19-H19	1.00(3)

The structure is characterized by the presence of tunnels with diameters of about 7.4 Å along the *c* axis where disordered solvent ethyl acetate molecules are located. They are surrounded by the lipophilic system of phenyls pointing in the direction of the tunnel center (see Figure 2). The large value of the tunnel diameter is in fact due to the hydrophobic external constituents. (However the disorder of the solvent molecules prevents further comments).

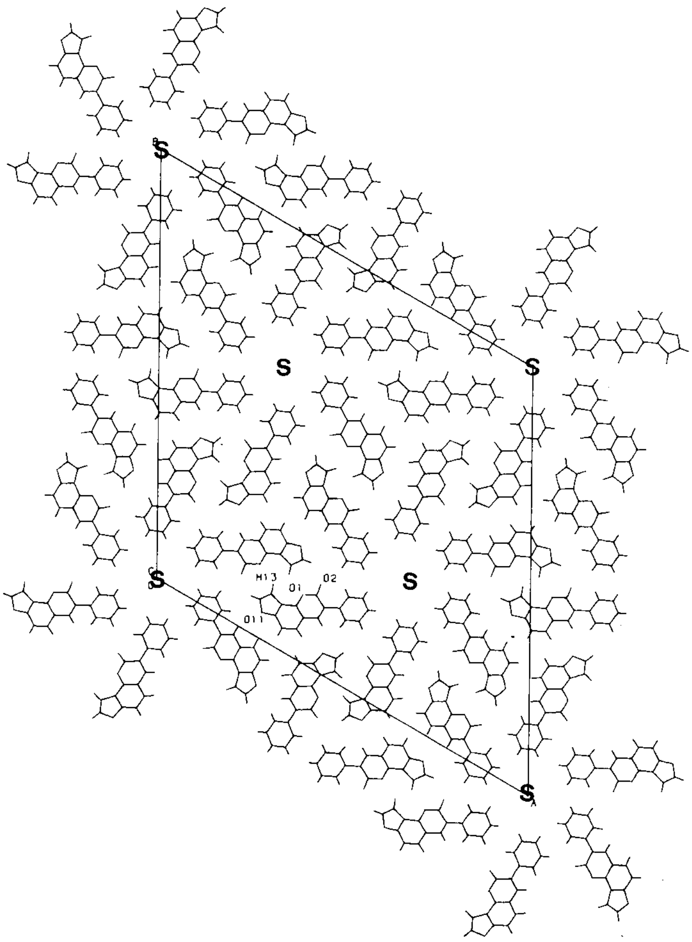


Figure 2. Packing diagram normal to the crystallographic c axis (hexagonal cell). (The disordered solvent molecules are indicated by S).

Bond distances and angles in the structure have the usual values found in angelicin [8], in *N,N*-dimethyl-4-amino-3-chloroangelicin [9], and in 3-chloro-5,6-dihydro-4-methylphenylaminoangelicin [10] (for the comparable part of the molecules).

EXPERIMENTAL

The uv spectra were measured in 95% ethanol with a Perkin-Elmer Model 550 S spectrophotometer. The ir spectra were taken in chloroform on a Perkin-Elmer model 398 spectrophotometer; the nmr spectra were recorded in deuteriochloroform on a Perkin-Elmer R-100 (60 MHz) and a Varian Mat Model CH7A (80 MHz) instrument; TMS as internal standard, J in Hz. X-Ray diffraction data were obtained by a single crystal Philips PW 1100 four circle diffractometer computer controlled. Melting points were determined with a Mettler FP1 apparatus.

N,N-Disubstituted 4-Amino-3-chloro-3,4,5,6-tetrahydro-3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones **IId,f**.

A solution of 2-chloro-2-phenylacetyl chloride (1.66 g, 8.8 mmoles) in anhydrous toluene (30 ml) was added dropwise under dry nitrogen to a stirred, cooled (0°) solution of enaminones **Ia-g** [1] (6 mmoles) and triethylamine (0.91 g, 9 mmoles) in the same solvent (80 ml).

The reaction mixture was stirred at room temperature for a certain time (see Table I) and filtered.

The toluene solution was evaporated under reduced pressure and the residue was chromatographed on Florisil (100-200 mesh), using as eluants benzene and diethyl ether.

The benzene eluate gave 3-phenylangelicin **V** by evaporation of the solvent under reduced pressure and recrystallization of the residue from ethyl acetate, whereas the diethyl ether eluate afforded in the same way the adducts **IId,f** (Table I).

In all other cases, adducts **IIa-c,e,g** could not be separated from **V**, therefore the crude mixture was used in the dehydrochlorination step.

N,N-Disubstituted 4-Amino-5,6-dihydro-3-phenyl-2*H*[2,3-*h*]-1-benzopyran-2-ones **IIIa-g**.

A solution of DBN (1.24 g, 10 mmoles) in anhydrous toluene (10 ml) was slowly added to a solution of adducts **IIa,f** (5 mmoles), or impure **IIa-c,e,g** in the same solvent (60 ml).

The mixture was refluxed for 1 hour under dry nitrogen, cooled at 0° and poured into 1*N* hydrochloric acid (10 ml). The acid solution was extracted with toluene, the extracts were washed with water, dried (magnesium sulfate) and evaporated under reduced pressure.

In the case of adducts **IId,f,g**, the solid residue consisted essentially of dihydroangelicins **IIId,f,g**, which were purified by recrystallization from ethyl acetate (Table III).

In the other cases, **IIa-c,e**, the residue was chromatographed on neutral alumina (grade I), using as eluants diethyl ether and ethyl acetate; 3-phenylangelicin **V** was recovered from the diethyl ether eluate, whereas dihydroangelicins **IIIa-c,e** were obtained from the ethyl acetate eluate (Table II).

N,N-Disubstituted 4-Amino-3-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-ones (4-Amino-3-phenylangelicins) **IVa,d-g**.

A solution of DDQ (1.14 g, 5 mmoles) in anhydrous toluene (50 ml) was added dropwise under dry nitrogen to a refluxing and stirred solution of dihydroangelicins **IIIa,d-g** (5 mmoles) in anhydrous toluene (200 ml). The reaction mixture was further refluxed for a certain time (Table IV), cooled and filtered. The filtrate was washed three times with 1*N* sodium hydroxide, then once with water, dried (magnesium sulfate) and evaporated under reduced pressure. The residue was recrystallized from a suitable solvent (Table IV).

3-Phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-2-one (3-Phenylangelicin) **V**.

This compound was obtained as white needles, mp 165-166° from ethyl acetate (lit [7] mp 161-162°); uv (95% ethanol) λ max nm (log ϵ): 242 (4.32), 247 sh (4.30), 255 sh (4.20), 266 sh (3.83), 322 (4.15); ir (chloroform): ν max 1727, 1702, 1614 cm^{-1} (lit [7] 1725 cm^{-1}); nmr (deuteriochloroform): δ 7.15 (d, J = 2.1, CH-9), 7.43 (mc, CH-5 + CH-6 + 3 H ar *m,p*), 7.69 (d, J = 2.1, CH-8), 7.72 (mc, 2 H ar *o*), 7.90 (s, CH-4).

Anal. Calcd. for $C_{17}H_{10}O_3$: C, 77.85; H, 3.84. Found: C, 77.80; H, 3.95.

As somewhat different nmr data were reported elsewhere [7], additional evidence for this compound was searched. To a solution of **V** in deuteriochloroform (about 40 mg/ml) were added three aliquots of the lanthanide shift reagent [tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)ytterbium] [Yb(fod)$_3$], yielding Yb(fod)$_3$-substrate ratios (φ) of 0.1290, 0.2474 and 0.3607, respectively. When the chemical shifts were plotted *vs.* the φ values, straight lines were obtained, with intercepts supporting the nmr assignments reported above and with slopes as follows: 14.16 (2 CH *o*), 8.77 (CH-4), 4.13 (CH-5), 2.60 (2 CH *m*), 2.00 (CH-6), 1.59 (CH *p*), -1.33 (CH-8), -5.17 (CH-9). In the shifted spectra, CH-5 and CH-6 showed two doublets (J = 8.6).

X-Ray Crystallography.

Crystals of **V** were obtained from an ethyl acetate solution. A crystal of prismatic shape with dimensions 0.25 x 0.25 x 0.38 mm was mounted on a Philips PW 1100 four circle diffractometer with graphite monochromator using MoKα radiation (λ = 0.71069 Å). Cell dimensions were obtained by least squares refinement of the setting angles of 25 reflections with $18 \leq 2\theta \leq 28°$, a = b = 41.021(10), c = 3.888(2) Å, and Z = 18 (hexagonal axes). The crystals belong to the trigonal system, space group $R\bar{3}$. Intensity data were collected to 50° in 2θ [range of hkl (hexagonal axes) $-39 \leq h \leq 39, 0 \leq k \leq 39, 0 \leq l \leq 4$]. A total of 3065 reflections were measured with $\theta/2\theta$ scan method at a rate of 1.5°/minute over a scan range of 1° with backgrounds count of 10 seconds each. Instrument and crystal stability were checked by two standard reflections -1,7,1; 2,5,0 measured each 180 minutes. The structure was solved by direct methods using MAGEX program [11], refined by full matrix least squares with anisotropic thermal parameters for all the non hydrogen atoms, minimizing the function $\Sigma w(\Delta F)^2$ with w = 1. Hydrogen atoms positions, found from difference Fourier synthesis, were refined with individual isotropic parameters.

A difference Fourier synthesis carried out at the R value of 0.055 showed the presence of four residuals: two of 1 e/Å^3 and two of 0.5 e/Å^3. They were interpreted as disordered molecules of ethyl acetate (the presence of the solvent was also individuated by nmr technique), with the C=O bond along the *c* axis and the CH_3 and CH_2-CH_3 groups disordered around the same axis. The best result in the refinement was obtained considering a ratio 1 of **V** to 0.17 ethyl acetate. (In fact lying C=O on the threefold axis the positions on either side of this axis are alternatives in order to avoid impossible O...O and C...C contacts).

The final R value [$R = \Sigma(|Fo|-|Fc|)/\Sigma|Fo|$] was 0.034 for 1281 reflections with $I \geqq 2.5\ \sigma(I)$ and a goodness of fit of 1.5. The minimum and maximum peaks in the final difference map were 0.1 e/Å^3. The maximum shift /esd in the final refinement cycle was 0.3. Data processing and computation were carried out using the SHELX 76 program package [12], drawings were made with PLUTO [13] and geometrical calculations with PARST [14]. Scattering factors in the analytical form were taken from ref [15].

Acknowledgement.

The authors wish to thank Mr. A. Panaro for the microanalyses, Mr. F. Fasce and Mr. C. Rossi for the uv, ir and nmr spectra, and Mrs. M. Magnabosco for technical assistance.

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