ABSOLUTE COMFIGURATION OF BENEOCYCLOBUTENE HOMOISOFLAVANONES FROM MUSCARI SPECIES

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Abstract - The absolute configuration of benzocyclobutene homoisoflavanones isolated from <u>Muscari</u> species was determined by the use of CD and X-ray analysis.

In a previous paper¹ we have described the determination of the absolute configuration at the chiral centre C-3 of a series of homoisoflavanones with 3-benzyl-4-chromanone skeleton, isolated from <u>Muscari</u> species. The adopted procedure (see Chart 1) implied the conversion, by reduction of the keto group at position 4, of suitably derivatized homoisoflavanones into two epimeric 4-alcohols, the <u>p</u>-bromobenzoylation of the 4-OH and 5-OH groups of these latter, the determination of the absolute configuration at the new chiral centre C-4 of the two 4,5-di-<u>p</u>-bromobenzoates by application of the exciton coupling method, and the elucidation of the configuration at C-3 relative to C-4 by ¹H-nmr analysis. All 3-benzyl-4-chromanone homoisoflavanones were found to possess configuration R.



Besides 3-benzyl-4-chromanone homoisoflavanones, we have isolated² from the same source a group of homoisoflavanones (1-5) possessing a skeleton constituted of a benzocyclobutene system fused at the 3-position

of a 4-chromanone system. The absolute configuration of the chiral centre 3 of 1-4 had not been elucidated, as it was, on the other hand, for scillascillin 5 that had been already isolated long before³ from a different plant. A procedure similar to that used for 3-benzyl-4-chromanones has now been applied to the elucidation of the absolute configuration of benzocyclobutene homoisoflavanones.



OCH3 H

12 OH



	R	R ₂	R3	R4	R5		R ₁	R2	R3
1	Он	он	оснз	он	н	7	p-Br-BzO	p-Br-BzO	н
2	ОН	OCH3	он	он	н	8	p-Br-BzO	н	p-Br-BzO
3	он	OCH3	ОН	OCH3	н	10	он	н	н
4	ОН	он	он	OCH3	н	11	p-Br-BzO	н	н
5	он	ОН	0-CH	12-0	н				
6	он	осн3	OCH3	OCH3	н				
9	p-Br-BzO	OCH3	OCH3	осн3	н				

Upon treatment with diazomethane in ether, the hydroxyl groups of homoisoflavanones 1, 2, 3, and 4, with the exception of the 5-OH chelated with the (4)C=0 group,⁴ were converted into methoxyl groups, affording the same destrorotatory 7,3',4'-tri-Q-methylated compound 6. Therefore, all four compounds 1-4 possess the same configuration.

OCH3 OH

Sodium borohydride reduction of compound 6 at the (4)C=0 group and subsequent esterification by treatment with p-bromobenzoyl chloride gave the mixture of two 4-epimeric 4,5-di-p-bromobenzoates. The most abundant of the two compounds succeeded in being isolated by TLC.

Identification of the <u>cis</u>- or <u>trans</u>-relationship occurring between the $4-0COC_6H_4Br$ and the (9)CH₂ groups in the isolated compound was attained through analysis of its ¹H-nmr spectrum (Table 1). This requested consideration of the ring-C conformational mobility, as depicted in Chart 2, where both possibilities for the configuration at the position 4 are represented (7 and 8), whereas the 3-centre is depicted with the configuration that later on was actually ascertained.

A four-bonding W-coupling (1.7 Hz) was observed (Table 1) to occur

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Chart 2 (R = p-Br-C_6H_4-CO-)
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between the 2-proton responsible of the higher-field (δ 4.2) double doublet and the 4-proton doublet (δ 6.37). This requested that the latter is oriented pseudo-equatorially as in the <u>c</u> conformation of the <u>cis</u> 4-epimer 7 or in the <u>t</u> conformation of the <u>trans</u> 4-epimer 8.

In the spectrum of the compound, a second W-coupling was observed to occur between the lower-field (δ 4.65) 2-proton signal and the 9-proton signal at δ 2.96. This is consistent only with the isolated di-p-bromobenzoates being the trans-isomer **s** in the $\underline{t_1}$ conformation, since in the <u>cis</u> 7 neither 2-proton is W-arranged together with either 9-proton, whereas in conformation $\underline{t_1}$ of the <u>trans</u>-epimer a near-coplanar W-arrangement can be seen for the 2-proton not W-coupled with the 4-H and the 9-proton oriented towards the 4-H.

The relative configuration of the chiral centres 3 and 4 of the pure 4,5-di-p-bromobenzoate having been ascertained this way, the absolute configuration R at C-4, as depicted in **8** (Chart 2), was established from the negative sign af the A-value (-46.8) of the split Cotton effects exhibited by the compound, that indicated the counter-clockwise arrangement of the two p-bromobenzoate chromophores. Consequently, the C-3 centre possesses the R-configuration. The identical configuration must be also possessed by the parent natural homoisoflavanones 1-4.

The circular dichroism curves of compounds 1-3 exhibited a positive Cotton effect at 290-292 nm and a negative Cotton effect at 333-337 nm (Table 2), that therefore may be taken as indicative of the R-configuration at C-3. This configuration must also be assigned to scillascillin 5, whose CD curve (Table 2) appeared to be similar to those of 1-3.

Table 1. ¹ H-nmr data in COCl ₃ .							
	2-CH2	4-CH/4-CH2	9-CH2	6-H, 8-H	21-11	51-H	Others
6	4.56, 4.60 AB (11.0 Hz)		3.06, 3.64 AB (14.0 Nz)	6.06, 6.10 AB (2.1 Hz)	6.65 ^b s	6.80 ^b в	3.63 s, 3.85 s, 3.87 s 3 x oc <u>H</u> 3
8	4.20 dd (11.1, 1.7 Hz) 4.65 dd (11.1, 1.0 Hz)	6.37 d (1.7 Hz)	2.96 dd (14.1, 1.0 Hz) 3.19 d (14.1 Hz)	6.41, 6.48 AB (2.5 Hz)	6.22 ^b s	6.74 ^b s	3.81 s, 3.82 s, 3.82 s 3 x OCH ₂ 7.51 d, 7.55 d, 7.75 d, 7.81 d (8.9 Hz) 2 x BrC ₆ H ₆ COO-
9	4.60, 4.63 AB (11.0 Hz)		2.98, 3.56 AB (14.0 Hz)	6.42, 6.49 AB (2.4 Hz)	6.62 ^b s	6.73 ^b s	3.80 s, 3.83 s, 3.89 s 3 x OCM_{π} 7.61 d, 8.04 d, (8.7 Mz) src _{gMg} COO-
10	4.17 s	2.86, 2.94 AB (16 Hz)	2.93, 3.12 AB (13.8 Hz)	6.03, 6.12 AB (2 Hz)	6.60 ^b s	6.78 ^b s	3.76 s, 3.82 s, 3.87 s 3 x OCH ₃
11	4.18. 4.22 AB (11.0 Hz)	2.77, 2.89 AB (16 Hz)	2.90, 3.11 AB (14.0 Hz)	6.39, 6.45 AB (2.3 Hz)	6.59 ^b s	6.75 ^b s	3.80 s, 3.81 s, 3.85 s 3 x OCH ₃ 7.63 d, 8.03 d, (8.7 Mz) src _e H ₄ COO-

The assignment of the absolute configuration to the above homoisoflavanones 1-5 was confirmed through X-ray analysis of a crystalline derivative prepared from 6. Compound 6 was converted by p-bromobenzoylation into ester 9. Sodium borohydride reduction of 9 unexpectedly gave the 4-deoxy 5-hydroxy compound 10 (¹H-nmr: (4)CH₂ ABq at δ 2.86, 2.94. MS:328 m/z),

Table	2. CD data of 1-3,	5, and 12 in NeON
	λ _{ext} , m	[0]
1	333 290	-6,800 +20,500
2	337 292	-9,000 +28,800
3	335 290	-16,500 +46,800
5	332 296	-20,400 +56,000
12	336 290	-5,900 +12,500

probably due to the shift of the <u>p</u>-bromobenzoyl group from the 5- to the 4-oxygen and subsequent hydrogenolysis of the group at that benzylic position. Anyway, <u>p</u>-bromobenzoylation of **10** gave **11**, whose crystals, grown from methanol as needles, were submitted to X-ray analysis, which allowed to determine unambiguously the absolute stereochemistry of the compound (Fig. 1).

The structure was solved by Patterson and Fourier techniques and refined to a conventional R index of 0.035 and a weighted R_w index of 0.042. The opposite enantiomorph was also refined and the conventional and the weighted indices were 0.043 and 0.052, respectively, at convergence.







Figure 1 - Perspective view showing the correct absolute Figure 2 - Perspective view of the two independent and isoconfiguration of 11 together with the atom labelling scheme. oriented molecules of the compound 12, in the correct absolute configuration together with the atom Labelling

The corresponding Hamilton's ratios⁵ 1.229 and 1.238 indicate, with a very high statistical significance, the chirality of C-3 as R.

The molecule can be shortly described as an assembly of three roughly planar fragments, stiffened by extended # electron charges. Apart from C(20), a C(2) and C(3), which are respectively 0.172(4), 0.226(4) and 0.519(3) Å out of the best plane, the chromanone fused system is planar within 0.024(4) Å. The dihydro- γ -pyrone ring displays a nearly perfect half-chair conformation with the following values of the ring puckering parameters according to Cremer and Pople⁶ for the sequence O(1)-C(9)-C(10)-C(4)-C(3)-C(2): Q (puckering amplitude) = 0.487(4) Å, Θ = 51.9(7)', $\phi = 259(1)$ '. The di-methoxy-benzo-cyclo-butene fragment, planar within 0.057(4) Å and with a slight bend around the fusion bond C(12)-C(13), is almost perpendicular to the chromanone system [interplanar angle = 82.9(1)']. The p-bromo-benzoate group also fulfils the condition of planarity with the outermost atoms Br and C(5) displaying the largest displacements of 0.047(1) and 0.054(4) λ , respectively. This plane, too, is almost perpendicular to the chromanone system [interplanar angle = 84.7(1) .

Homoisoflavanone 12, isolated² from bulbs of <u>Muscari comosum</u>, can also be assumed to possess R-configuration, as a positive Cotton effect at 290 nm and a negative Cotton effect at 336 nm were observed in its CD

^a Labelling of **11** as in Figure 1.

Table 3. Observed and calculated values of $\Delta F = F_{\perp} - F_{\perp} $ for the correct absolute configuration of 12						
h	k	ι	∆۶°	∆⊧c		
-5	-2	1	0.47	0.25		
-3	-3	10	0.14	0.17		
-2	-4	5	-0.12	-0.19		
-2	-4	6	0.38	0.14		
0	-3	8	0.29	0.22		
2	-3	8	0.12	-0.12		
3	•1	2	-0.08	-0.22		
3	-3	0	-0.12	-0.14		
4	-1	3	-0.09	-0.18		
4	-7	10	-0.26	-0.10		
5	-5	4	0.20	0.12		
6	-4	3	0.39	0.14		
6	-2	8	0.36	0.11		
7	-2	1	0.28	0.11		
8	-4	6	-0.28	-0.12		

Table 4. Crystal data				
	Compound 11	Compound 12		
Crystal dimensions, mm	0.10x0.20x0.50	0.07x0.14x0.42		
Formula	C26 ^H 23 ^O 6 ^{Br}	C1806 [№] 16		
Formula weight	511.4	328.3		
Space group	P2,2,2	P2,		
a, A	7.431(1)	10.246(4)		
b, Å	11.736(2)	10.344(1)		
c, Å	26.492(4)	14.673(5)		
β, *_	-	101.49(2)		
v, 4 ³	2310.5(7)	1523.9(8)		
Z	4	4 (2 mols <u>per</u>		
-		asym. unit)		
D ₂ , g/cm ³	1.470	1.431		
<i>X</i> Cu-Kα, Å	1.5418	1.5418		
θ _{max} (*)	76	76		
Absorption coefficient (μ), cm ⁻¹	27.6	8.6		
No. indep. refl.	2772	3357		
No. refl. above 3σ(1)	2530	3023		
R	0.035	0.035		
R	0.042	0.047		
R ² (inverted structure)	0.043	0.036		
R_{W}^{-} (inverted structure)	0.052	0.047		

curve. However, because of the different substitution pattern of the ring B, confirmatory evidence for this assumption was searched from X-ray analysis of the compound recrystallized from methanol. The structure was solved by direct methods using MULTAN80⁷ and refined to R = 0.035 and $R_{w} =$ 0.047. Two independent molecules with the same configuration at C-3 are contained in the asymmetric unit. In this case the lack of strong anomalous scatterers prevent the use of the Hamilton's test as a discriminator for the determination of the correct absolute structure. The problem was solved by the Bijvoet difference method. 15 Friedel pairs with Fo differing significantly at the end of the refinement were remeasured with great care. The agreement, shown in Table 3, between observed and calculated ΔF for the structure containing molecules with R-configuration gives an enough clear evidence that this structure, to which the drawing in Fig. 2 and the coordinates of Table 6 refer, is that with the correct absolute configuration. The two independent molecules show a close correspondence in bond lengths and angles, except three valency angles involving C(3).^b These differences are connected to a remarkable conformational variation occurring in the central fragment made up by the dihydro-y-pyrone and cyclo-butene rings. It is allowed by the flexibility

^b Labelling of **12** as in Figure 2.

Table 5
Table 5

Fractional atomic coordinates and equivalent isotropic thermal parameters (λ^{2}) of the non-hydrogen atoms with the e.s.d.'s in parameters for the compound 11.

_	$= \frac{\mathbf{s}_{eq} + \frac{4}{3} \mathbf{\Sigma}_{i} \mathbf{\Sigma}_{j} \mathbf{\varepsilon}_{ij} \mathbf{s}_{i} \mathbf{s}_{i}}{\mathbf{s}_{ij} \mathbf{s}_{ij} \mathbf{s}_{ij} \mathbf{s}_{ij}}$						
	x	y y	z	Beq			
Br	0.24894(6)	0.09543(4)	0.04509(1)	6.187(9)			
0(1)	1.3138(3)	0.2712(2)	-0.24124(9)	4.76(3)			
0(2)	1.3032(4)	-0.1244(2)	-0,2481(1)	5.43(6)			
0(3)	0.7204(4)	0.0628(3)	-0.17541(9)	7.26(8)			
0(4)	0.9484(3)	0.0685(2)	-0.12121(8)	4.13(4)			
0(5)	0.9292(4)	0.7560(2)	-0.10658(9)	5.54(6)			
0(6)	1.2106(4)	0.7679(2)	-0.0523(1)	6.05(6)			
C(2)	1.2364(6)	0.3779(3)	-0.2256(1)	4.60(7)			
C(3)	1.2006(5)	0.3796(3)	-0.1689(1)	4.27(7)			
C(4)	1.0692(5)	0.2862(3)	-0.1560(1)	4.48(7)			
C(5)	1.0681(4)	0.0701(3)	-0.1633(1)	3.91(6)			
C(6)	1.1239(5)	-0.0332(3)	-0.1823(1)	4.16(7)			
C(7)	1.2436(5)	-0.0301(3)	-0,2231(1)	4.25(6)			
C(8)	1.3020(4)	0.0724(3)	-0.2422(1)	4.22(6)			
C(9)	1.2454(5)	0.1734(3)	-0.2206(1)	4.01(6)			
C(10)	1.1252(4)	0.1752(3)	-0.1799(1)	3.83(6)			
C(11)	1.3786(5)	0.3867(3)	-0.1365(1)	4.86(8)			
C(12)	1.3077(5)	0.5020(3)	-0.1188(1)	4.48(7)			
C(13)	1.1546(5)	0.4968(3)	-0.1475(1)	4.33(7)			
C(14)	1.0196(5)	0.5770(3)	-0.1462(1)	4.63(7)			
C(15)	1.0474(5)	0.6676(3)	-0.1130(1)	4.51(7)			
C(16)	1.2051(5)	0.6745(3)	-0.0631(1)	4.72(7)			
C(17)	1.3379(5)	0.5916(3)	-0.0854(1)	4.95(8)			
C(18)	1.3543(7)	0.7716(4)	-0.0165(2)	7.4(1)			
C(19)	0.7591(6)	0.7478(4)	-0.1308(2)	6.3(1)			
C(20)	1.2659(6)	-0.2337(3)	-0.2268(2)	5.77(9)			
C(21)	0.7722(4)	0.0664(3)	-0.1330(1)	4.25(6)			
C(22)	0.6543(4)	0.0714(3)	-0.0879(1)	3.91(6)			
C(23)	0.4723(5)	0.0680(4)	-0.0963(1)	5.8(1)			
C(24)	0.3519(5)	0.0746(5)	-0.0571(1)	6.1(1)			
C(25)	0.4157(5)	0.0856(3)	-0,0092(1)	4.43(7)			
C(26)	0.5963(5)	0.0870(4)	0.0007(1)	5.30(8)			
C(27)	0.7172(5)	0.0798(4)	-0.0389(1)	5.13(8)			

Fractional atomic coopdinates and equivalent isotropic thermal parameters (A^{2}) of the non-hydrogen atoms with the e.s.d.'s in parantheses for the compound 12.							
$\mathbf{B}_{eq} = \frac{4/3}{2} \mathbf{I}_{j} \mathbf{I}_{j} \mathbf{A}_{j} \mathbf{A}_{j}$							
x y z ⁸ eq							
0(1)	1.0335(2)	-0.3609	0.7491(2)	3.60(5)			
0(2)	0.7450(2)	-0.0809(3)	0.6847(2)	4.43(6)			
0(3)	0.8507(3)	0.0356(3)	0.8401(2)	5.29(6)			
0(4)	1.2135(3)	-0.1632(5)	1.05/1(2)	4.76(6)			
0(5)	0.7007(2)	-0.4017(3)	0.0040(1)	3.02(3)			
C(2)	0.9757(3)	-0.3320(4)	0.6538(2)	3.37(7)			
C(3)	0.8343(3)	-0.2829(3)	0.6437(2)	3.23(7)			
C(4)	0.8320(3)	-0.1653(4)	0.7049(2)	3.36(4)			
C(5)	0.9387(3)	-0.0635(4)	0.8574(3)	3.85(7)			
C(6)	1.0311(4)	-0.0660(4)	0.9388(3)	4.39(8)			
C(7)	1.1222(3)	-0.1676(4)	0.9559(2)	3.77(7)			
C(8)	1.1213(4)	-0.2675(4)	0.8915(2)	3.65(7)			
C(Y)	1.0280(3)	-0.2023(3)	0.8099(2)	3.10(0)			
C(10)	0.7527(3)	-0.1053(4)	0.7072(2)	3.27(0)			
C(12)	0.6845(3)	-0.3933(4)	0.5561(2)	3.57(7)			
C(13)	0.7561(3)	-0.3919(3)	0.6517(2)	3.11(6)			
C(14)	0.7074(3)	-0.4848(3)	0.7116(2)	3.00(6)			
C(15)	0.6223(3)	-0.5843(4)	0.6698(2)	3.39(7)			
C(16)	0.5720(4)	-0.5880(4)	0.5741(3)	3.94(8)			
C(17)	0.6036(4)	-0.4912(4)	0.5152(3)	4.16(8)			
C(18)	0.545/(4)	-0.7979(4)	0.0959(3)	5.26(9)			
0(1)	1.3130(4)	-0.2010(4)	1.0318(3)	4,/4(Y) I 49/5)			
0(2')	1.2881(3)	0.0930(3)	0.7990(2)	4.41(6)			
0(31)	1,1962(3)	-0.0607(3)	0.6628(2)	4.38(6)			
0(41)	0.8054(3)	0.0519(3)	0.4563(2)	3.97(5)			
0(51)	1.2077(3)	0.1786(3)	1.0319(2)	4.21(5)			
0(6')	1.3996(3)	0.2879(3)	1.1566(2)	4.88(6)			
C(2')	1.0332(3)	0.52/5(4)	0.8100(2)	3.45(7)			
	1.1/94(3)	0.2941(3)	0.8185(2)	3.19(0)			
0(5)	1 0030/3)	0.1049(4)	0.7732(2)	3.20(7)			
C(6')	0.9994(3)	-0.0009(4)	0.5597(2)	3.52(7)			
C(7')	0.8939(3)	0.0859(4)	0.5341(2)	3.25(6)			
C(8')	0.8834(3)	0.1968(4)	0.5855(2)	3.34(7)			
C(9')	0.9781(3)	0.2184(3)	0.6653(2)	3.16(6)			
C(10')	1.0869(3)	0.1345(3)	0.6941(2)	3.04(6)			
C(11')	1.2691(4)	0.4031(4)	0.7842(2)	3.83(7)			
0(12')	1.3419(3)	0.4112(4)	U.8856(3)	3.72(7)			
C(13')	1.2042(3)	0.3133(3)	1.0044/25	3.21(0)			
0(151)	1 3867(3)	0.2(30(3)	1.0040(2)	3.23(7)			
C(16')	1.4635(4)	0.4320(4)	1.0390(3)	6.30(8)			
C(17')	1.4424(4)	0.4725(4)	0.9454(3)	4.31(8)			
C(181)	1.5112(4)	0.3255(6)	1.2236(3)	5.67(9)			
C(19')	0.6971(4)	0.1382(4)	0.4223(3)	4.72(9)			

Table 6

of the dihydro- γ -pyrone ring and is due to packing requirements. In both molecules the dihydro- γ -pyrone ring adopts a sofa conformation with C(2) out of the chromanone plane but on the opposite sides in the two cases. The ring puckering parameters for the sequence O(1)-C(9)-C(10)-C(4)-C(3)-C(2) are : Q = 0.466(4) Å, Θ = 125.0(7)*, ϕ = 110(1)* for the unprimed molecule and Q = 0.462(4) Å, Θ = 55.4(7)*, ϕ = 286(1)* for the primed molecule.

The primed molecule appear to be more regular and consists essentially of two roughly planar atomic distributions: the chromanone system and the benzo-<u>cyclo</u>-butene moiety. Their interplanar angle is $78.0(2)^{\circ}$. Moreover, the skeleton of the primed molecule is conformationally congruent with that of the molecule of **11**. The unprimed molecule, instead, exhibits a strong distorsion localized at the <u>cyclo</u>-butene fragment. In both molecules there is an omologous strong intramolecular H-bond between O(3) and O(2) (see Table 8).

EXPERIMENTAL

Nmr spectra were recorded at 400.13 (¹H) and 100.75 (¹³C) MHz with a 400-AM FT spectromer (Bruker). CD curves were measured with a Jasco J-600 dichrograph. Mass spectra were recorded with a Kratos MS50 instrument. PLC was performed on precoated silica gel layers Merck F_{254} , 0.5 mm.

<u>Methyl derivative</u> 6. Samples (ca. 20 mg) of 1, 2, 3 and 4 were separately treated with a solution of diazomethane in ether for 48 h at r.t.. PLC (5:3:2 hexane-dioxane-ether, 2 runs) of the crude products obtained after usual work-up gave pure dextrorotatory 6 (15+18 mg) in all cases. ¹H-nmr: Table 1.

<u>p-Bromobenzoate</u> §. 6 (30 mg) was treated in methanol with sodium borohydride for 10' at 0°C. The crude product, obtained by addition of acetic acid, evaporation of the solvent and extraction with ethyl acetate, was treated with <u>p</u>-bromobenzoyl chloride in anhydrous pyridine for 24 h at r.t.. Usual work-up and PLC (98:2 benzene-ethyl acetate) gave pure 8 (19 mg). ¹H-nmr: Table 1. CD (methanol): $\Delta\epsilon_{239} = +18.9$, $\Delta\epsilon_{245} = 0$, $\Delta\epsilon_{254} =$ -27.9, A-value = -46.8.

<u>p-Bromobenzoate 11.</u> 6 (11 mg) was treated with <u>p</u>-bromobenzoyl chloride in anhydrous pyridine for 24 h at r.t.. Usual work-up gave <u>p</u>-bromobenzoate 9 (11 mg); ¹H-nmr: Table 1. Treatment of 9 (10 mg) with sodium borohydride in methanol as above afforded 10 (8 mg); ¹H-nmr: Table 1; EIMS 70 eV: 328 <u>m/z</u> (M⁺). <u>p</u>-Bromobenzoylation of 10 (6 mg) as above and PLC (9:1 benzene-ethyl acetate) gave 11 (6 mg); ¹H-nmr: Table 1. ¹³C-nmr (CDCl₃): δ 30.1 and 40.2 (CH₂-4 and CH₂-9); 44.7 (C-3); 55.6, 56.5 and 56.6 (3xOCH₃); 72.9 (CH₂-2); 100.0 and 101.4 (CH-6 and CH-8); 106.1 and 108.5 (CH-2' and CH-5'); 102.4 (C-4a); 128.3 and 129.0 (C-Br and C-C=0); 131.8 and 132.1 (4xCH of <u>p</u>-bromobenzoyl group); 135.3 (C-1'); 140.2 (C-6'); 150.1, 150.3 and 150.9 (C-3', C-5 and C-4); 156.3 and 159.4 (C-7 and C-8a); 163.1 (C=0).

X-Ray Analyses.

Crystal data and relevant details of the structure determinations for the compounds 11 and 12 are presented in Table 4. The final atomic parameters of 11 and 12 are given in Tables 5 and 6 while the values of the bond lengths and angles are reported in Tables 7 and 8.

An Enraf-Nonius CAD4 diffractometer on line with a VAX 750 computer was

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Table 7	
Bond lengths (Å) and	relevant valence
angles (°) with thei	re.s.d.'s in
parentheses for the c	ompound 11.
0(1)-C(2)	1.440(5)
0(1)-C(9)	1.369(4)
C(2)-C(3)	1.525(5)
C(3)-C(4)	1.506(5)
C(4)-C(10)	1.506(5)
C(10)-C(9)	1.400(5)
C(10)-C(5)	1.376(5)
C(3)-C(6) C(6)-C(7) C(7)-C(8) C(3)-C(13) C(3)-C(13) C(11)-C(12) C(12)-C(13) C(12)-C(14)	1.376(5) 1.376(5) 1.376(5) 1.362(5) 1.526(5) 1.526(6) 1.370(5)
C(13)-C(15) C(15)-C(15) C(15)-C(16) C(16)-C(17) C(17)-C(12) C(16)-O(6) O(6)-C(18) C(15)-O(5) O(5)-C(19)	1.396(5) 1.416(6) 1.387(6) 1.392(6) 1.368(5) 1.429(6) 1.370(5) 1.421(7)
C(7)-O(2)	1.364(5)
O(2)-C(20)	1.428(5)
C(5)-O(4)	1.427(4)
O(4)-C(21)	1.346(5)
C(21)-O(3)	1.188(5)
C(22)-C(22)	1.482(5)
C(22)-C(23)	1.371(5)
C(23)-C(24)	1.374(5)
C(24)-C(25)	1.360(6)
C(25)-C(26)	1.367(6)
C(26)-C(27)	1.384(5)
C(27)-C(22)	1.384(5)
C(25)-Br	1.902(4)
O(1)-C(2)-C(3)	111.4(3)
C(2)-C(3)-C(4)	109.1(3)
C(3)-C(4)-C(10)	110.8(3)
C(4)-C(10)-C(9)	120.8(3)
C(10)-C(9)-0(1)	122.2(3)
C(9)-0(1)-C(2)	117.7(3)
C(9)-C(10)-C(5)	115.4(3)
C(10)-C(5)-C(6)	125.4(3)
C(5)-C(6)-C(7)	116.8(4)
C(5)-C(6)-C(7)-C(8)	120.5(3)
C(7)-C(8)-C(9)	120.1(3)
C(8)-C(9)-C(10)	121.8(3)
C(2)-C(3)-C(11)	113.0(4)
C(2)-C(3)-C(13)	114.6(3)
C(4)-C(3)-C(13)	117.2(3)
C(4)-C(3)-C(13)	115.2(3)
C(11)-C(3)-C(13)	86.5(3)
C(3)-C(11)-C(12)	85.7(3)
C(11)-C(12)-C(13) C(12)-C(13)-C(3) C(3)-C(13)-C(14) C(12)-C(13)-C(14) C(12)-C(13)-C(14) C(13)-C(12)-C(17) C(13)-C(12)-C(17) C(13)-C(14)-C(15) C(14)-C(15)-C(16) C(15)-C(16)-C(17) C(15)-C(16)-C(17)	94.4(3) 93.5(3) 142.2(4) 124.1(4) 124.0(4) 121.4(4) 115.5(4) 121.2(4) 121.6(4)

Table 8					
Bond lengths (Å) and relevant valence angles (°) with their e. s. d.'s in parentheses for the compound 12.					
	Unprimed molecule	Primed molecule			
0(1)-C(2) 0(1)-C(9) C(2)-C(3) C(4)-C(10) C(10)-C(9) C(10)-C(5) C(5)-C(6) C(4)-C(7) C(7)-C(8) C(1)-C(1) C(1)-C(1) <tr< th=""><th>1.436(3) 1.363(3) 1.514(3) 1.514(4) 1.514(4) 1.440(3) 1.440(3) 1.430(4) 1.398(4) 1.398(4) 1.398(4) 1.373(4) 1.532(4) 1.532(4) 1.532(4) 1.532(4) 1.397(3) 1.397(3) 1.409(3) 1.409(3) 1.409(3) 1.431(4) 1.356(3) 1.431(4) 1.436(3)</th><th>1.441(3) 1.364(3) 1.517(3) 1.517(3) 1.447(3) 1.447(3) 1.427(3) 1.398(4) 1.398(4) 1.398(4) 1.398(4) 1.598(5) 1.598(5) 1.598(5) 1.528(3) 1.598(4) 1.513(3) 1.527(5) 1.433(4) 1.357(5) 1.575(5) 1.575(5) 1.577(</th></tr<>	1.436(3) 1.363(3) 1.514(3) 1.514(4) 1.514(4) 1.440(3) 1.440(3) 1.430(4) 1.398(4) 1.398(4) 1.398(4) 1.373(4) 1.532(4) 1.532(4) 1.532(4) 1.532(4) 1.397(3) 1.397(3) 1.409(3) 1.409(3) 1.409(3) 1.431(4) 1.356(3) 1.431(4) 1.436(3)	1.441(3) 1.364(3) 1.517(3) 1.517(3) 1.447(3) 1.447(3) 1.427(3) 1.398(4) 1.398(4) 1.398(4) 1.398(4) 1.598(5) 1.598(5) 1.598(5) 1.528(3) 1.598(4) 1.513(3) 1.527(5) 1.433(4) 1.357(5) 1.575(5) 1.575(5) 1.577(
C(13)-U(8) D(6)-C(18) O(3)O(2) H(03)O(2)	1.3/5(3) 1.424(4) 2.616(3) 1.74(2)	1.378(3) 1,406(4) 2,580(3) 1,89(2)			
0(1)-C(2)-C(3) C(2)-C(3)-C(4) C(3)-C(4)-C(10) C(4)-C(10)-C(9) C(10)-C(9)-O(1) C(9)-O(1)-C(2) C(9)-O(1)-C(5) C(9)-C(10)-C(5) C(10)-C(5)-C(6) C(5)-C(6)-C(7) C(6)-C(7)-C(8) C(1)-C(8)-C(9)-C(10) C(2)-C(3)-C(13) C(2)-C(3)-C(13) C(1)-C(3)-C(13) C(1)-C(3)-C(13) C(1)-C(3)-C(13) C(1)-C(12)-C(13) C(1)-C(12)-C(13) C(1)-C(12)-C(13) C(1)-C(12)-C(13) C(1)-C(12)-C(13) C(1)-C(12)-C(13) C(1)-C(12)-C(13) C(1)-C(12)-C(13) C(1)-C(12)-C(13) C(13)-C(14)-C(15) C(13)-C(14)-C(15) C(14)-C(17)-C(12) C(17)-C(12)-C(17) C(13)-C(16)-C(17) C(13)-C(16)-C(17) C(13)-C(16)-C(17) C(13)-C(17)-C(12) C(17)-C(12)-C(17) C(13)-C(16)-C(17)-C(12) C(17)-C(12)-C(17)-C(12)-C(17) C(13)-C(14)-C(15)-C(16)-C(17)-C(12)-C(111.5(2) 109.8(2) 115.2(2) 121.5(2) 121.5(2) 121.5(2) 121.5(2) 121.4(2) 116.3(2) 121.4(2) 118.1(2) 122.2(2) 118.7(2) 117.2(2) 86.5(2) 93.5(2) 93.5(2) 93.5(2) 93.5(2) 93.5(2) 93.5(2) 117.2(2) 86.5(2) 93.5(2) 117.2(2) 86.5(2) 93.5(2) 117.2(2) 86.5(2) 117.2(2) 86.5(2) 117.2(2) 117.2(2) 86.5(2) 117.2(2)	112.0(2) 109.3(2) 115.7(2) 121.4(2) 121.4(2) 121.4(2) 116.9(2) 121.6(2) 121.6(2) 121.6(2) 118.4(2) 122.3(2) 118.4(2) 118.4(2) 112.6(2) 115.7(2) 114.8(2) 115.9(2) 85.9(2) 85.9(2) 85.9(2) 93.3(2) 94.7(2) 142.7(2) 122.6(2) 142.7(2) 122.6(2) 135.5(2) 121.8(2) 121.8(2) 121.8(2) 121.8(3) 1			

used for the data collections with the ω/Θ scan technique at room temperature. The intensities were corrected for Lorentz and polarization factors and for the absorption effects by the empirical correction according to North et al..⁸ The refinement of the positional and anisotropic thermal parameters for non-hydrogen atoms was carried out by full-matrix (on F) least-squares cycles. The H atoms were generated at their expected positions taking into account the indications of the difference Fourier map for the methyl and hydroxyl groups. All the H-atoms were included, using a riding model, in the last refinement with the isotropic thermal parameter slightly larger than the B_{eq} of the carrier atoms. For both compounds the refined parameters included an overall scale factor and the positional and anisotropic thermal parameters of the non-drogen atoms. In particular, for 11 the refinement included also a correction for the secondary extinction $[g = 9.9(5)x10^{-7}]$. The weighting scheme, according to Killean and Lawrence⁹ was 1/w = $[\sigma^2(F_0) + (0.02 \times F_0)^2 + 1]$ and the absolute value of the highest positive or negative peaks in the final difference Fourier map was not larger than 0.3 e λ^{-3} . For the compound 12, the weighting scheme was $1/w = \sigma^2(F_0)$ and the positive and negative heights in the final difference map did not exceed 0.16 and 0.18 e λ^{-3} , respectively. Atomic scattering factors and anomalous dispersion corrections were taken from international Tables for X-ray Crystallography¹⁰. The Enraf-Nonius package of computer programs (SDP) was used. Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited at the Dipartimento di Chimica of the University of Naples and are available from F.G..

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REFERENCES

- 1. H. Adinolfi, G. Barone, H. H. Corsaro, L. Hangoni, R. Lanzetta, and H. Parrilli, Tetrahadron, 44, 4981 (1988).
- 2. G. Barone, H. H. Corsaro, R. Lanzetta, and H. Parrilli, Phytochemistry, 24, 921 (1988) and references cited therein.
- 3. 1. Kuono, T. Komori, and T. Kawasaki, Tetrahedron Letters, 46, 4569 (1973).
- 4. W. Heiler and C. Thamm, Fortschr. Chem. Org. Naturst., 40, 105 (1981).
- 5. W. C. Hamilton, <u>Acta Crystellogr</u>., 18, 502, 1965.
- 6. D. Cremer and J. A. Pople, <u>J. Am. Chem. Soc</u>., 97, 1354, 1975.
- 7. Nain, P., Fiske, S. J., Hull, S. E., Lessinger, L., Genmain, G., Declercq, J.-P. & Woolfson, N. N. (1980) MULTAN80. <u>A</u> <u>System of Computer Programs for the Automatic Solutions of Crystal Structures from X-ray Diffraction Date</u>. Univs. of York, England, and Louvain, Belgium.
- 8. A. C. T. North, D. C. Phillips and F. S. Mathews, Acta Crystallogr., A24, 351, 1968.
- 9. R. C. G. Killean and J. L. Lawrence, Acta Crystallogr., 825, 1750, 1969.
- 10. "International Tables for X-ray Crystallography", Vol IV, Kynoch Press, Birmingham, England, 1974.