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New Nitrogenous and Aromatic Derivatives from *Aglaia argentea* and *A. forbesii*

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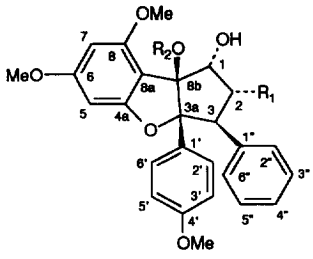
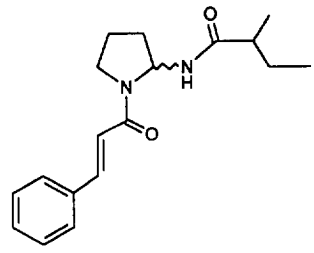
Abstract. Seeds and leaves of *Aglaia argentea* and bark of *A. forbesii* were extracted. The known cyclopentatetrahydrobenzofuran derivative rocaglaol (**1**) and the aminopyrrolidine odorine (**5**), were isolated together with nine new compounds : didesmethylrocaglamide (**6**), aglains A (**7**), B (**8**) and C (**9**), aglaforbesins A (**10**) and B (**11**), ethylrocaglaol (**12**) and forbaglins A (**13**) and B (**14**). Compounds **7-11** and **13,14** possess a new cyclopentatetrahydrobenzopyran and benzoxepine skeleton, respectively, linked to an odorine type moiety. All the structures were elucidated notably by 2D NMR spectroscopy. In addition, the structure of forbaglin A was established by X-Ray crystallographic analysis. Didesmethylrocaglamide revealed strong cytotoxic activity against KB cells (IC_{50} 0.006 µg/ml). Copyright © 1996 Elsevier Science Ltd

Aromatic compounds showing a cyclopentatetrahydrobenzofuran skeleton, rocaglaol (**1**) and the cytotoxic compounds rocaglamide (**2**) and its congeners, desmethylrocaglamide (**3**) and methylrocaglate (**4**), have been previously isolated from three species of the genus *Aglaia A. elliptica*, *A. odorata* and *A. roxburghiana*.[2,3,4] The two latter species also yielded a nitrogenous compound named odorine or roxburghiline (**5**),[5,6] which possesses a 2-aminopyrrolidine ring linked by two amide functions to 2-methylbutyric acid and cinnamic acid, respectively. We have isolated **1** from the bark of *A. forbesii* King. and **5**[7] from the leaves of *A. argentea* Bl.. In addition, nine new compounds were obtained. *A. argentea* yielded didesmethylrocaglamide (**6**) and three compounds having a related cyclopentatetrahydrobenzopyran skeleton linked to a 2-aminopyrrolidine moiety similar to the one of odorine : aglains A (**7**), B (**8**) and C (**9**)[8]. The bark of *A. forbesii* also contained **7** and the related compounds aglaforbesins A (**10**) and B (**11**), together with ethylrocaglaol (**12**) and two nitrogenous aromatic derivatives named forbaglin A (**13**) and forbaglin B (**14**). Compounds **13** and **14** contain a benzoxepine ring which was also linked to an odorine type moiety. Only one of the new compounds, didesmethylrocaglamide **6**, showed strong cytotoxic activity against KB cells with an IC_{50} of 0.006 µg/ml, which is of the same order of magnitude than rocaglamide. Structural identification was achieved using spectroscopic methods, essentially 2D NMR. The structure of **13** was further established by X-Ray crystallographic analysis.

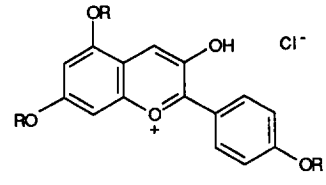
All compounds were obtained from plant materials collected in Malaysia[9] by extraction with ethanol. Odorine (**5**), didesmethylrocaglamide (**6**), aglains A (**7**) B (**8**) and C (**9**) were obtained from the crude extracts of *A. argentea* after successive CC and PTLC on silica gel. The ethanol extract of the bark of *A. forbesii* was partitioned between water and CH_2Cl_2. Rocaglaol (**1**), aglain A, aglaforbesins A (**10**) and B (**11**),



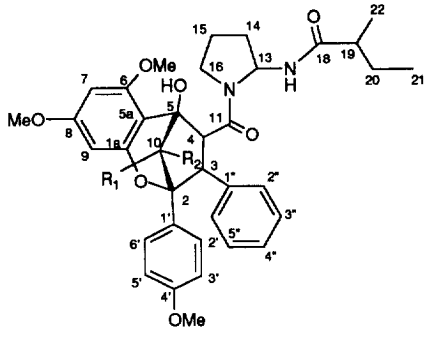
1 $R_1 = R_2 = H$
2 $R_1 = CONMe_2$, $R_2 = H$
3 $R_1 = CONHMe$, $R_2 = H$
4 $R_1 = COOMe$, $R_2 = H$
6 $R_1 = CONH_2$, $R_2 = H$
12 $R_1 = H$, $R_2 = Et$



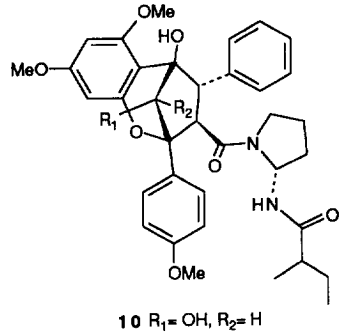
5



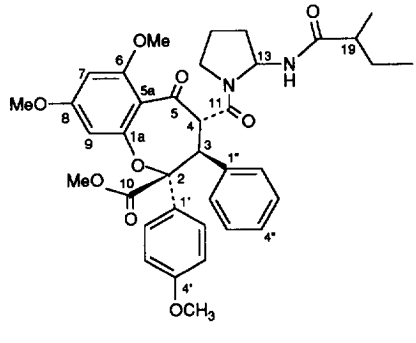
16 R = H
17 R = Me



7 R_1 = OAc, R_2 = H, H -3β, H -4α, 13S
8 R_1 = H, R_2 = OH, H -3β, H -4α, 13S
9 R_1 = H, R_2 = OH, H -3α, H - 4 β, 13S
15 R_1 = H, R_2 = OAc, H -3α, H -4β, 13S



10 R_1 = OH, R_2 = H
11 R_1 = H, R_2 = OH



13 13R, 19S
14 13S

ethylrocaglaol (**12**) and forbaglins A (**13**) and B (**14**) were obtained from the organic extract by repeated CC and PTLC.

Didesmethylrocaglamide (**6**), $[\alpha]_D$ - 44°, gave a M^+ peak in the HREIMS at *m/z* 477.1764 (Δ -2.35 mmu) corresponding to the molecular formula of $C_{27}H_{27}NO_7$. In the IR spectrum, the amide band appeared at 1650 cm^{-1}. The ^1H NMR spectrum showed three MeO groups at δ 3.60, 3.76 and 3.78. In addition, signals of three aromatic rings similar to those of rocaglamide **2** and desmethylrocaglamide **3** were observed, i.e. two meta coupled aromatic protons at δ 6.10 and 6.22 (2d, *J* = 2 Hz), the characteristic AA'BB' system of a *p*-disubstituted benzene ring at δ 6.55 and 7.08 and the signals of a monosubstituted benzene ring (5H, m, δ 6.92). The spectrum further exhibited signals at δ 4.72 (d, *J* = 6 Hz), 3.82 (dd, *J* = 6 and 14 Hz) and 4.21 (d, *J* =14 Hz) typical of H-1, H-2 and H-3 of desmethylrocaglamide **3**. The ^{13}C NMR was also similar to the ones of **2** and **3** showing the signals of a tetrasubstituted, a disubstituted and a monosubstituted benzene ring (see experimental), an amide C=O group at δ 172.9 and the two characteristic quaternary carbons 3a and 8b at δ 102.1 and 93.3. Thus, owing the elemental composition and the lack of NMe group, **6** was assigned the structure of didesmethylrocaglamide.

Aglain A (**7**) , $[\alpha]_D$ + 8°, exhibited a $[M+Na]^+$ peak at *m/z* 695.2927 (Δ -1.8 mmu) in the HRFABMS, which matched the molecular formula of $C_{38}H_{44}N_2O_9$. The IR spectrum showed bands at 1747, 1650 and 1622 cm^{-1} corresponding to an ester and two amide functions, respectively. The ^1H NMR spectrum disclosed three MeO groups and three benzene rings similar to **6** (Table 1), hence indicating a structurally related aromatic moiety. In addition, the signals of a 2-methylbutyric amide and a 2-aminopyrrolidine ring reminiscent of the one reported for odorine were observed (Table 1), suggesting that part of the odorine structure could be linked through an amide function to an acid moiety of the rocaglamide type instead of the NMe_2 group. The ^1H NMR spectrum also showed three signals of methine protons at δ 6.44, 3.95 and 4.41 which could correspond to the 1, 2 and 3 position in rocaglamide. The low field shift of the proton at δ 6.44 suggested that it was α to an OAc group, which was observed at δ_H 1.85, δ_C 20.2 and at δ_C 171.0. However, the coupling patterns of the three protons differed from those of **6**. The proton at δ 6.44 appeared as a sharp singlet while the two others were coupled together (*J* = 8 Hz). Furthermore, the signals of the quaternary carbons C-3a and C-8b with typical chemical shifts present in **6** were lacking and replaced by two quaternary carbon signals at δ 86.3 and 79.6. These ^1H and ^{13}C NMR data suggested that aglain A has the formula depicted in **7** showing a pyran ring in place of the furan of rocaglamide. In the HMBC experiment (Table 1), the cross peaks H-10/C-5,C-5a, H-4/C-5,C-5a, and H-3/C-2,C-5 supported the relative positions 2,3,4,5 and 10, whereas the correlations from H-4 to C-11 and from H-3 to C-2"6" indicated the connectivities of C-4 to C-11 and of C-3 to the monosubstituted aromatic ring, respectively. The NOESY relationships H-3/H-10, H-3/H-2"6", H-3/H-2'6', H-4/H-2"6" further confirmed these assignments and established the relative configuration at C-2, C-3, C-4, C-5 and C-10 as depicted in formula **7**. In addition, the NOESY spectrum (Table 1) displayed the cross peaks H-4/H-13 and H-21/H-2"6". The latter indicated that the pyrrolidine ring and the chain adopted a preferred conformation, where the chain is placed near the monosubstituted benzene ring. Further scrutiny of a Dreiding model showed that in such a conformation a NOE may be observed only if the configuration at C-13 is S.[10]

Aglain B (**8**), $[\alpha]_D$ +10°, gave a MH^+ peak at *m/z* 631 in the CIMS that is 42 amu less than aglain A. Accurate mass measurement confirmed the molecular formula of $C_{36}H_{42}N_2O_8$ (631.3035 MH^+, Δ 1.6 mmu) corresponding to the one of a deacetylaglain A. The IR spectrum showed two amide bands at 1672 and 1624 cm^{-1}. The ^{13}C NMR data (Table 2) were similar to those of aglain A (**7**) except for C-4 and C-10, which were

shifted downfield. The HMBC correlations (Table 2), which were also similar to those of **7** (Table 1), supported the attachment of the benzyl ring and the amide group at C-3 and C-4, respectively. NOESY correlations were observed between H-3 and OH-10 as well as between H-4 and H-2"6", indicating the same H-3β and H-4α configuration as in **7**, but a reversed configuration at C-10. In addition, the NOESY cross peaks H-4/H-13 and H-21/H-2"6" indicated a 13S configuration.[10]

Aglain C (**9**), $[\alpha]_D$ -105 °, was an isomer of **8**, showing a $[M+Na]^+$ peak in the HRFABMS at *m/z* 653.2778 (Δ 6.1 mmu), which matched the molecular formula of $C_{36}H_{42}N_2O_8$. The IR spectrum exhibited two amide absorptions at 1650 and 1622 cm^{-1}. The 1D NMR and HMBC data were similar to those of **8** (Table 2). However the stereochemistry at C-3 and C-4 was reversed as compared with **7** and **8**, and the configuration at C-10 was identical to the one of **8**, since the NOESY correlations H-4/OH-10 and H-4/H-2"6" were observed. These assignments were confirmed by the cross peaks appearing betweeen the methyl of the acetyl group and H-2"6" in the NOESY spectrum of the acetate **15**, which was prepared by acetylation of **9**. Finally, the correlations H-4/H-13 and H-21/H-2"6" in the NOESY spectrum of **9** and **15** indicated a 13S configuration.[10]

Aglaforbesin A (**10**), $[\alpha]_D$ -18°, was an isomer of **8** and **9**, which disclosed an MH^+ peak at *m/z* 631.3025 (Δ 0.6 mmu) in the HRCIMS, corresponding to the molecular formula of $C_{36}H_{42}N_2O_8$. The IR spectrum showed two amide absorptions at 1656 and 1625 cm^{-1}. The NMR spectra exhibited signals which were similar to those of **9** (Table 3). However, the HMBC experiment (Table 2) clearly indicated that **10** was a positional isomer of **7-9**, since the same correlations H-10/C-5,C-5a, H-4/C-5,C-5a, and H-3/C-2,C-5 as before were observed, together with correlations between H-3 and C-11 and H-4 and 2"6". The NOESY relationships H-4/H-10 and H-3/H-2"6" established the configuration at C-3, C-4 and C-10 as depicted. The configuration at C-4 was further supported by the highfield shift of MeO-6 (δ 3.11) since it was placed inside the shielding zone of the unsubstituted benzene ring at C-4α. The molecular model further revealed that the observed NOESY correlations H-3/H-13 and H-21/H-2"6" indicated a 13R configuration.[10]

Aglaforbesin B (**11**), $[\alpha]_D$ +1°, was also an isomer of **8**, showing a MH^+ peak at *m/z* 631.2999 (Δ -2.0 mmu) in the HRCIMS, which matched the molecular formula of $C_{36}H_{42}N_2O_8$. The IR spectrum exhibited two amide absorptions at 1658 and 1616 cm^{-1}. The HMBC experiment (Table 3) indicated the same position at C-3 and C-4 of the odorine chain and the benzene ring, respectively, as in aglaforbesin A (**10**). MeO-6 was shifted downfield thus revealing that the benzene ring was at C-4α. However, the lack of NOE between H-10 and H-4 suggested that aglaforbesin B was epimeric at C-10 with aglaforbesin A. Aglaforbesin B possessed also a 13R configuration, which was supported by the NOESY correlation H-3/H-13 and H-21/H-2"6" and hence was assigned structure **11**.[10]

Ethylrocaglaol (**12**), $[\alpha]_D$ -18°, showed an M^+ ion in the HREIMS at *m/z* 462.2021 (Δ -2.9 mmu) which was in agreement with the molecular formula $C_{28}H_{30}O_6$. The NMR spectra were similar to the ones of rocaglaol. The typical signals of the C_2H_5O group were observed at δ_C 14.5 and 59.3. In the COSY, H-1 at δ 4.94 was coupled to an OH at δ 4.05 indicating that the ethyl group was located at positon 8b.

Forbaglin A (**13**), mp 246°, $[\alpha]_D$ +58°, showed a MH^+ ion peak in the CIMS at *m/z* 659 corresponding to the molecular formula of $C_{37}H_{42}N_2O_9$. The IR spectrum exhibited carbonyl absorptions at 1760, 1680 and 1660 cm^{-1}. The ^1H NMR spectrum showed three MeO groups at δ 3.05, 3.62 and 3.80 and the signals of three aromatic rings similar to those of rocaglamide and aglain A (Table 4). The characteristic signals of an odorine type moiety were also present, with two carbonyl groups at δ 168.8 and 177.8. The ^{13}C NMR spectrum displayed two additional carbonyls at δ 194.7 and 171.6. The former could correspond to a conjugate keto

group and the latter to an ester, which gave an absorption band at 1760 cm^{-1} in the IR spectrum. An additional MeO at δ 3.05 in the ^1H NMR suggested the presence of a COOMe group. The high field value of the chemical shift could be explained by the shielding effect of the nearby aromatic rings. The spectrum also shows two protons at δ 4.70 and 5.26, which were coupled together (J = 10 Hz) and corresponded to methine carbons at δ 65.6 and 50.9, respectively. HMBC correlations from both protons and the C=O of odorine and from the proton at δ 5.26 with the 2"6" carbons of the monosubstituted aromatic ring indicated that the methine at δ 65.6 bore the odorine chain and the methine at δ 50.9 the aromatic ring, respectively. In addition the proton at δ 4.70 correlated with the ketonic carbonyl at δ 194.7, and the hydrogen at δ 5.26 showed a cross peak with a quarternary carbon at δ 91.6. These data were in agreement with formula **13**, but since no HMBC correlations were observed with the COOMe group, an X-Ray determination was undertaken in order to confirm the preceeding assumption.

The results (Fig. 1) established the definitive structure and relative stereochemistry of forbaglin A **13**[11]. The seven-membered ring adopts a twist-boat conformation where the phenyl rings are in an axial position. The aminopyrrolidine chain at C-4 is equatorial with the five membered ring in a half-chair conformation, while the 2-methylbutyryl chain at C-13 is pseudo-axial. In the crystal, this chain is spatially close to the phenyl ring at C-3 ($C_{20}...C_{6"}$: 4.303 Å, $C_{21}...C_{5"}$: 4.384 Å) and the terminal methyl group C-21 is in an extended conformation (C_{18}-C_{19}-C_{20}-C_{21} : 168°). Furthermore, the conformation of the pyrrolidine chain brings H-4 and H-13 near to each other ($H_4...H_{13}$: 2.40 Å; Fig. 1A).

The NOESY spectrum measured in CD_4O (Table 4) showed the correlation H-4/H13 and H-21/H2"6", which were in accordance with the conformation observed in the solid state. However, in order to observe the NOE between H-21 and H-2"6", a free rotation around the C_{19}-C_{20} single-bond has to occur, which would lead the terminal methyl group C-21 to occupy the gauche conformation (C_{18}-C_{19}-C_{20}-C_{21} : about 60°) bringing this methyl within 3.0 Å to the phenyl group. Such a rotation has been featured in Fig. 1B.

In addition, the ^1H NMR spectrum of **13** in CD_4O showed a doubling of the signals due to the presence of about 10% of a minor component. In $CDCl_3$, the ratio between the two components of the mixture was about 50/50. This was due to restricted rotation around the C_{11}-N_{12} bond, since in the NOESY spectrum (CD_4O) the relationship H4/H16 corresponding to a rotation of about 180° around the C_{11}-N_{12} bond was observed for the minor component.

Forbaglin B (**14**), $[\alpha]_D$ +76°, exhibited a MH^+ peak in the HRCIMS at m/z 659.2953 (Δ -1.6 mmu) which matched the molecular formula of $C_{37}H_{42}N_2O_9$. The IR spectrum displayed carbonyl absorptions similar to the ones of **13** at 1755, 1671 and 1650 cm^{-1}. The 1D NMR and the HMBC spectra (Table 4) were also similar. The same coupling pattern was observed for H-3 and H-4, whereas the NOESY spectrum showed cross peaks between H-3 and H-2'6' indicating the same stereochemistry at C-2, C-3 and C-4. The difference was the configuration at position 13, since the NOESY exhibited correlations between H-4 and H-13, and H-22 and MeO-6. Observation of the models indicated that such correlations involved a 13S stereochemistry.[10]

Biogenetically, aglains A, B, C (**7-9**) and aglaforbesins A and B (**10-11**) may derive from the flavonoid **17** and odorine by a cycloaddition reaction. The tridesmethylderivative of **17**, pelargonidine chloride (**16**), is a component of the acid hydrolysate of the water soluble part of *Aglaia forbesii* bark extract. Such a biogenetic origin could explain the various isomers which have been isolated. Furthermore, the forbaglins could derive from the aglain type compounds by an opening of the C_5-C_{10} bond followed by oxidation.

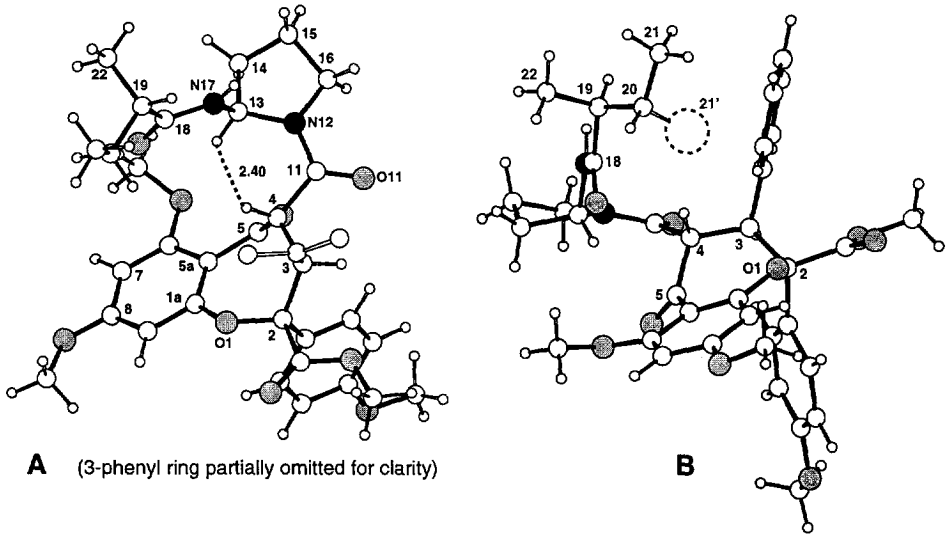


Fig.1. ORTEP plots of the X-Ray structure of forbaglin A (**13**).

Table 1. ^{13}C (75 MHz) and ^{1}H (400 MHz) NMR Data[a] for aglain A (**7**) (CD_4O)

position	δ C	δ H (*J* Hz)	HMBC	NOESY	position	δ C	δ H (*J* Hz)	HMBC	NOESY
1a	155.1				20	27.4	1.07 m	18,19,21,22	22
2	86.3				21	11.7	0.48 t (7.5)	19,20	2"6", 3"5"
3	56.0	4.41 d (5)	2,4,5,11,1"2"6"	10, 2'6, 2"6"	22	16.9	0.84 d (7)	18,19,20	
4	57.6	3.95 d (5)	3,5,5a,10,11,1"	13, 2"6"	1'	131.3			
5	79.6				2'6'	127.9	7.45 d (9)	2, 2'6', 4'	3', 5'
5a	108.0				3'5'	113.2	6.85 d (9)	1',3'5', 4'	OMe-4',2'6'
6	158.9				4'	160.1			
7	93.0	6.33 d (2)	5a, 6, 8, 9	MeO-6,MeO-8	1"	137.1			
8	162.0				2"6"	130.1	6.50 d (7)	2"6", 4"	21
9	93.0	6.04 d (2)	1a, 5a, 7, 8	2'6', MeO-8	3"5"	128.2	)		
10	74.2	6.44 s	5,5a,1', COMe	2'6'	4"	127.4	)6.98-7,06)	1",2"6",3"5"	21
11	171.9				MeO-6	56.3	4.03 s	6	
13	64.7	6.21 d (6)	11,14,15,16,18		MeO-8	55.5	3.77 s	8	
14	34.3	2.14 m 1.99 m	13,15,16 13,15,16	16	MeO-4'	55.2	3.77 s	4'	
15	21.7	2.00 m	14		COMe	171.0			
16	46.7	3.55 m	13,14,15	15	COMe	20.2	1.85 s		
18	177.7								
19	42.7	1.87 m	18, 20, 21, 22	20, 21, 22					

[a] assignments based on 2D experiments.

Table 2. ^{13}C (75 MHz) and ^{1}H NMR (400 MHz) Data[a] for aglain B (**8**) and aglain C (**9**)

	8				**9**[b]			
position	δ C[c]	δ H (*J* Hz)[c]	HMBC[c]	NOESY[b]	δ C	δ H (*J* Hz)	HMBC	NOESY
1a	154.3				153.9			
2	90.6				89.1			
3	56.3	4.90 d (5)	2,4,5,11,1",2"6"	2'6',2"6",OH_{10}	57.3	4.50 d (10)	2,4,11,1",2"6"	2'6', 2"6"
4	62.6	4.00 d	3,5, 5a, 11,1"	13, 2"6", NH	62.8	4.14 d (10)	3,5,5a, 11,1"	13,2"6",OH-10,NH
5	80.4				82.0			
5a	111.4				105.1			
6	157.6				157.9			
7	93.0	6.30 d (2)	5a, 8, 9	MeO-6, MeO-8	92.2	6.02 d (2)	5a,6,8,9	MeO-6
8	157.6				161.2			
9	94.5	6.10 d (2)	5a, 6, 7, 8	MeO-8	94.6	6.06 d (2)	5a,7,8	MeO-8
10	84.1	4.10 s	2, 3, 4, 5a		80.1	4.75 s	2, 3, 4, 5a	2'6', OH-10
11	174.2				169.9			
13	65.1	6.15 d (6)	15,16		63.5	6.54 m	15,16	14, NH
14	34.6	a 1.90 m b 2.10 m			34.5	2.00 m	13,15,16	13, 15ab
15	21.8	1.90 m		14a,16	21.7	a 1.95 m b 1.70 m	16	15b,16b 16a
16	47.1	3.55 m			44.2	a 3.19 m b 3.60 m	13,14	16b
18	177.5				175.5			
19	42.7	1.80 m	18,20,21,22	NH	42.4	1.74 m	18,20,21,22	22, NH
20	27.8	a 1.25 m b 1.35 m	18,19,21, 22 18,19,21, 22		26.7	a 1.25 m b 1.35 m	18,19,21, 22 18,19,21, 22	
21	11.6	0.75 m	19, 20	2"6", 3"5"	11.7	0.75 t (7)	19, 20	2"6", 3"5"
22	16.9	0.75 m	18, 19, 20		16.8	0.80 d (7)	18, 19, 20	
1'	130.8				130.3			
2',6'	129.1	7.60 d (9)	2, 2'6', 4'		130.5	7.38 d (9)	2,1', 4'	
3'5'	113.6	6.90 d (9)	4'		112.9	6.60 d (9)	1', 2'6', 4'	MeO-4'
4'	160.0				158.7			
1"	138.2				142.0			
2",6"	130.3	6.85 m	3		130.5.	7.10 m	3,4"	
3",5"	128.1	)) 7.05 m			128.0	))6.95 m	))1", 2"6"	
4"	128.4	)			129.5	)	)	
MeO-6	56.3	3.75 s	6		56.1	3.76 s	6	
MeO-8	55.3	4.05 s	8		55.4	3.70 s	8	
MeO-4'	55.2	3.75 s	4'		55.2	3.65 s	4'	3'5'
OH-5 OH-10 NH						5.70 s 3.85 s 5.30 d (6)	5, 5a, 10 2, 5, 10 18	

[a]assignments based on 2D experiments. [b]in CD_4O. [c]in $CDCl_3$ (OH-5 δ 5.70 s, OH-10 δ 5.32 s, NH δ 5.28 d J = 6 Hz)

Table 3. ^{13}C (75 MHz) and ^{1}H (400 MHz) NMR Data[a] for aglaforbesin A (**10**) and aglaforbesin B (**11**) (CD_4O)

	10				**11**			
position	δ C	δ H (*J* Hz)	HMBC	NOESY	δ C	δ H (*J* Hz)	HMBC	NOESY
1a	155.2				154.2			
2	87.4				88.0			
3	57.1	3.72 d (10)	2,4,10,11,1"	13, 2"6"	58.0	3.90 d (10)	2,4,11,1"	13, 2"6"
4	58.6	4.05 d (10)	3,5,5a,10,11,1",2"	10, 2"6"	58.5	4.70 d (10)	3,5,5a,11,1",2"6"	2"6"
5	83.3				84.0			
5a	106.8				109.0			
6	162.6				161.0			
7	94.9	5.98 d (2)	5a, 6,8,	MeO-6,MeO-8	94.5	5.95 d (2)	5a,6,8,9	MeO-6,MeO-8
8	163.2				163.0			
9	97.1	6.45 d (2)	1a,5a, 7, 8	MeO-8	97.0	6.42 d (2)	1a,5a,7,8	22, MeO-8
10	77.4	4.48 s	4, 5, 5a	2'6'	82.0.	4.13 s	3, 4, 5a	2'6'
11	171.9				171.5			
13	66.1	5.55 m	11,14,15,16,18	3,14ab,2'6'	66.0	5,40 d (5)	11,15,16,18	14ab, 2'6'
14	35.1	a 1.55 m b 1.00 m	13,15,16 13,15	14b 13	35,0	0.82 m 1.48 m	13,15 13,15,16	14b 13,15,16ab
15	22.4	1.52 m	14,16	16ab	22.0	a 1.5 m	14	16ab
16	47.7	3.18 m 2.58 m	14	15 15	47.4	a 2.70 m b 3.25 m	15 14	16b
18	179.1				178.5			
19	44.0	1.70 m	18,20,21,22		43.5	2.10 m	18,20,22	20,21,22
20	28.3	a 1.50 m b 1.30 m	18,19,21, 22 18,19,21, 22		29.5	a 1.35 m b 1.50 m	18,19,21, 22 18,19,21, 22	22
21	13.3	0.80 t (7)	19, 20	2"6", 3"5",4"	12.5	0.79 t (7)	19,20	20, 3'5'
22	18.9	0.95 d (7)	18, 19, 20		18.0	0, 97 d (7)	18, 19, 20	2"6",3"5",4"
1'	131.4				130.5			
2',6'	129.4	7.70 d (9)	2, 3'5', 4'	3'5'	130.0	7.84 d (9)	2,2'6', 4'	3'5'
3'5'	115.3	6.98 d (9)	1',2'6', 4'	MeO-4'	104.0	6.95 d	1', 2'6', 4'	
4'	161.8				161.5			
1"	139.3				139.5			
2",6"	130.9	6.88 m	4,3"5",4"		131.0.	6.95 m	3,3"5",1"	3"5"
3",5"	129.6	)	3"5"		129.0	)	)	
4"	129.0	) 7.13 m)	2"6"		131.0	)7.16m)	)1", 2"6")	
MeO-6	57.1	3.11 s	6		56.5	3.10 s	6	
MeO-8	56.8	3.80 s	8		56.4	3.81 s	8	
MeO-4'	56.8	3.81 s	4'		56.4	3.82 s	4'	

[a]assignments based on 2D experiments.

Table 4. ^{13}C (75 MHz) and ^{1}H (400 MHz) NMR Data[a] for forbaglin A (**13**) and forbaglin B (**14**) (CD_4O)

	13				**14**			
position	δ C	δ H (*J* Hz)	HMBC	NOESY	δ C	δ H (*J* Hz)	HMBC	NOESY
1a	160.0				162.2			
2	91.6				92.5			
3	50.9	5.26 d (10)	2,4,11,1",2"6"	4,2'6',2"6"	54.0	5.00 d (10)	2,4,11,1",2"6"	2'6'
4	65.6	4.70 d (10)	3,5,11,1"	13,2"6"	65.5	4.67 d (10)	3,5,11,1"	13
5	194.7				192.5			
5a	114.9				115.4			
6	160.5				162.2			
7	94.5	6.16 d (2)	5a,6,8,9	MeO-6, MeO-8	96.2	6.12 d (2)	5a,6,8,9	MeO-6,MeO-8
8	165.6				166.4			
9	99.2	6.60 d (2)	1a,5a,7,8	MeO-8	101.6	6.60 d (2)	1a,5a,7,8	MeO-8, 2'6'
10	171.6				172.5			
11	168.6				169.1			
13	64.4	5.10 d (5)	14,15,16	4,14ab	64.6	5.12 br d	14,15,16	4,14
14	34.1	a 1.80 m b 1.60 m		13,14b 13,14a	36.0	1.45 m	13,15,16	13, 15ab
15	21.6	1.80 m		14a,16	23.0	a 1.60 m b 1.85 m		15b, 16a 15a, 16b
16	46.9	3.35 m	14, 15	15	48.0	a 3.10 m b 3.47 m	14, 15a 14, 15b	15a 15b, 16a
18	177.8				178.7			
19	42.7	1.90 q (7)	18,20,21,22		43.0	1.80 q (6.7)	18,20,21,22	
20	27.4	a 1.40 m b 1.25 m	18,19,21, 22 18,19,21, 22		29.4	a 1.20 m b 1.35 m	18,19,21, 22 18,19,21, 22	
21	12.2	0.70 t (7)	19, 20	2"6", 3"5"	12.4	0.75 t (7.4)	19, 20	
22	17.3	0.85 d (7)	18, 19, 20		16.8	0.47 d (6.7)	18, 19, 20	7,20ab,MeO-6
1'	128.0				129.0			
2',6'	130.1	7.34 d (9)		3	131.0	7.38 d (9)	2'6', 4'	3
3'5'	114.6	6.70 d (9)	1', 4'	MeO-4'	115.5	6.73 d (9)	1', 4', 3'5'	2'6', MeO-4'
4'	161.1				162.0			
1"	141.1				142.0			
2",6"	130.8	7.60 d (8)	3, 2"6",3"5",4"	3, 4, 10, 21	129.0	7.32 m	2"6", 4"	
3",5"	128.9	)) 7.26 m	2"6"	)) 2'6'	131.5	7.27 m	1", 3"5"	
4"	128.4	)		)	129.5	7.20 m	2"6"	
MeO-6	55.9	3.62 s	6		57.0	3.60 s	6	7
MeO-8	56.3	3.8O s	8		57.0	3.83 s	8	7, 9
MeO-10	52.3	3.05 s	10		53.3	3.12 s	10	2'6'
MeO-4'	56.3	3.62 s	4'		56.4	3.70 s	4'	3'5'

[a] assignments based on 2D experiments.

EXPERIMENTAL

General. Optical rotations at 20° were taken on a Perkin-Elmer 241 polarimeter. Spectra were recorded as follow : UV (MeOH), Shimadzu UV-161 UV-visible spectrophotometer; IR, Nicolet 205 FT-IR spectrometer; EIMS (70 eV), Kratos MS 50; CIMS, Kratos MS9; FABMS, HREIMS, HRCIMS, Kratos, MS 80; HRFABMS, VG-Zab-Seq spectrometer; NMR, Bruker AC 250, AC 300 or AM 400 spectrometer; HPLC, Waters Associated Instrument.

Plant material. Seeds and leaves of *Aglaia argentea* Bl. and bark of *A. forbesii* King. were collected in Dungun, Terengganu, Malaysia, on 22 March, 1993. Identification was made by one of us (G.P.). Voucher specimens of *A. argentea* (KL 4347) and *A. forbesii* (KL 4339) are deposited at the Laboratoire de Phanérogamie, Muséum National d'Histoire Naturelle in Paris, at the Herbarium of Department of Chemistry, University of Malaya, Kuala Lumpur, Malaysia and at the Herbarium of the Forest Research Institute, Kepong, Malaysia.

Extraction and isolation. The dried ground seeds of *Aglaia argentea* Bl (250 g) were extracted exhaustively with EtOH at room temperature. The extract (7.6 g) was chromatographed on silica gel (Merck H 60) with mixtures of CH_2Cl_2-MeOH as eluent. The fractions, which were eluted with CH_2Cl_2-MeOH 98:2 and 95:5, yielded the apotirucallanes gentinones A, B, C and D[12]. A small further fraction eluted with CH_2Cl_2-MeOH 95:5 (0.64 g) was purified by PTLC yielding **6**.

The dried ground leaves of *Aglaia argentea* (200 g) were extracted with EtOH at room temperature. The extract (19.6 g) was chromatographed on silica gel (70-200 mesh) with mixtures of CH_2Cl_2-MeOH as eluent. A fraction (4.43 g), which was eluted with CH_2Cl_2-MeOH 95:5, was subjected to further silica gel (Merck H 60) CC chromatography followed by PTLC yielding aglain C (**9**) (41 mg) i) CC CH_2Cl_2-MeOH, 98:2 ii) CC CH_2Cl_2-MeOH 95:5 iii) PTLC CH_2Cl_2-MeOH 98:2, odorine (**5**) (40 mg) i) CC CH_2Cl_2-MeOH 98: 2 ii) CC hexane-Me_2CO 85:25, aglain A (**7**) (47 mg) i) CC CH_2Cl_2-MeOH 98:2 ii) CC hexane-Me_2CO 85:35 iii) PTLC hexane-Me_2CO 60:40, aglain B (**9**) (50 mg) i) CC CH_2Cl_2-MeOH 98:2 ii) CC hexane-Me_2CO 85:35 iii) PTLC hexane-Me_2CO 50:50.

The dried ground bark of *Aglaia forbesii* King. was extracted with EtOH. The extract (53.1 g) was dissolved in MeOH and partitioned between water and CH_2Cl_2. The organic extract (3.22 g) was subjected to repeated silica gel (Merck H 60) chromatography and PTLC yielding ethylrocaglaol (**12**) (10 mg) i) CC CH_2Cl_2MeOH 95:5 ii) CC cyclohexane-MeOH 95:5 iii) PTLC hexane-Me_2CO 60:40 i) CC CH_2Cl_2-MeOH 95:5 ii) CC cyclohexane-MeOH (95:5) iii) PTLC hexane-Me_2CO 60:40 (57 mg), rocaglaol (**1**) (60 mg) i) CC CH_2Cl_2-MeOH 98:2 ii) CC cyclohexane-EtOAc 70:30, aglain A (**7**) (40 mg) i) CC CH_2Cl_2-MeOH 95:5 ii) CC cyclohexane-MeOH 95:5 iii) PTLC hexane-Me_2CO 60:40, aglaforbesin B (**11**) (20 mg) i) CC CH_2Cl_2-MeOH 98:2 ii) CC cyclohexane-MeOH 98:2 iii) PTLC hexane-Me_2CO 60:40, forbaglin A (**13**) (150 mg) i) CC CH_2Cl_2-MeOH 95:5 ii) CC cyclohexane-MeOH 95:5 iii) PTLC hexane-Me_2CO 60-40, aglaforbesin A (**10**) 40 mg i) CC CH_2Cl_2-MeOH 95:5 ii) CC cyclohexane-MeOH 95:5 iii) PTLC hexane-Me_2CO 60:40 and forbaglin B (**14**) (3 mg) i) CC CH_2Cl_2-MeOH 95:5 ii) PTLC cyclohexane-MeOH 95:5. iii) PTLC hexane-Me_2CO 60:40. The H_2O extract (1 g) was refluxed with HCl 6N (5 ml) for 1 h. After evaporation under vacuum, the residue was submitted to HPLC analysis on a reverse phase column (Novapack C18, eluent MeOH/H_2O 45:55. Pelargonidine chloride (**16**) was identified by k' and UV comparison with an authentic sample of **16**.

Didesmethylrocaglamide (**6**). Amorphous, $[\alpha]_D$ -44 ($CHCl_3$, c = 1). UV λ max nm 230 (sh, log ε 4.05), 272 (log ε 3.02). IR ν_{max} cm^{-1} 3518, 3412, 1675, 1600. EIMS *m/z* (rel. int) 477 (10) (M^+), 459 (10), 442 (10), 300 (100). ^1H NMR (CD_3OD, 300 MHz) δ 3.60 (3H, s, OMe-4'), 3.76, 3.78 (3H x 2, 3s, OMe-6 and OMe-8), 3.82 (1H, dd, J = 14 and 6 Hz, H-2), 4.21 (1H, d, J = 14 Hz, H-3), 4.72 (1H, d, J = 6 Hz, H-

1), 6.10 (1H, d, J = 2 Hz, H-7), 6.22 (1H, d, J = 2 Hz, H-5), 6.55 (2H, d, J = 9 Hz, H-3'5'), 6.92 (5H, m, H-2"6", H-3"5", H-4"), 7.08 (2H, d, J = 9 Hz, H-2'6'). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 52.0 (C-2), 55.4, 56.0, 56.6 (3 x OMe), 79.2 (C-1), 89.5 (C-5), 92.7 (C-7), 93.3 (C-8b), 102.1 (C-3a), 107.5 (C-8a) 113.2 (C-3'5'), 127.1 (C-4"), 128.2, 128.6, 129.2 (C-2'6', C-2"6", C-3"5"), 129.2 (C-1'), 136.4 (C-1"), 157.6, 159.1, 161.4, 164.4 (C-4a, C-6, C-8, C-4'), 172.9 (CO).

Aglain A (**7**). Amorphous powder $[\alpha]_D$ -8 (MeOH, c = 1). UV λ max nm 272 (log ε 3.60). IR ν_{max} cm^{-1} 3518, 3412, 1747, 1650, 1622, 1581. FABMS *m/z* 695 $[M+Na]^+$. ^1H and ^{13}C NMR see Table 1.

Aglain B (**8**). **8** Amorphous, $[\alpha]_D$ -10 (MeOH, c = 1). UV λ max nm 272 (log ε 3.41). IR ν_{max} cm^{-1} 3481, 3440, 1672, 1624, 1587. CIMS *m/z* 631 $[MH]^+$. ^1H and ^{13}C NMR see Table 2.

Aglain C (**9**). **9** was recrystallised from MeOH, mp 180°, $[\alpha]_D$ -105° ($CHCl_3$, c =1); UV λ max nm 271 (log ε 3.27); IR ν_{max} cm^{-1} 3428, 3442, 1650, 1622, 1596. FABMS *m/z* 653 $[M + Na]^+$; *m/z* 637 $[M + Li]^+$. ^1H and ^{13}C NMR see Table 2.

Aglaforbesin A (**10**). Amorphous, $[\alpha]_D$ -18 (MeOH, c = 1). UV λ max nm 271 (log ε 3.25). IR ν_{max} cm^{-1} 3668, 3575, 1656, 1625, 1581. CIMS *m/z* 631 $[MH]^+$. ^1H and ^{13}C NMR see Table 3.

Aglaforbesin B (**11**). Amorphous, $[\alpha]_D$ +1 (MeOH, c = 1). UV λ max nm 270 (log ε 3.25) δ IR ν_{max} cm^{-1} : 3500, 3450, 1658, 1616, 1581. CIMS *m/z* 631 $(MH)^+$. ^1H and ^{13}C NMR see Table 3.

Ethylrocaglaol (**12**). Amorphous, $[\alpha]_D$ -18 (MeOH, c = 1). UV λ max nm 272 (log ε 3.46). EIMS *m/z* (rel. int) 462 (10) (M^+), 341, 300, 134, 91. ^1H NMR ($CDCl_3$ 300 MHz) δ 0.69 (3H, t, J = 7 Hz, H-10), 1.95 (1H, dd, J = 7 and 14 Hz, H-2β), 2.40 (1H, m, H-9β), 2.64 (2H, m, H-9α and H-2α), 3.75 (3H, s, OMe-4'), 3.85 (1H, m, H-3), 3.85 (3H, s, OMe-8), 3.88 (3H, s, OMe-6), 4.05 (1H, s, OH-1), 4.94 (1H, d, J = 7 Hz, H-1), 6.19 (1H, d, J = 2 Hz, H-7), 6.32 (1H, d, J = 2 Hz, H-5), 6.70 (2H, d, J = 9 Hz, H-3'5'), 6.80 (2H, m, H-2"6"), 7.08 (3H, m, H-3"5", H-4"), 7.18 (2H, d, J = 9 Hz, H-2'6'). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 14.47 (C-10), 35.3 (C-2), 53.5 (C-3), 54.8, 55.4, 55.5 (3 x OMe), 59.34 (C-9), 79.9 (C-1), 89.5 (C-5), 92.0 (C-7), 99.9, 101.1, 104.9 (C-3a, C-8a, C-8b), 112.0 (C-3'5'), 126.2 (C-4"), 127.2, 127.9, 128.5 (C-2'6', C-2"6", C-3"5"), 128.0 (C-1'), 137.8 (C-1"), 157.1 (C-8), 158.2 (C-4'), 161.0 (C-4a), 163.6 (C-6).

Forbaglin A (**13**). **13** was recrystallised from MeOH, mp 246°, $[\alpha]_D$ +58 (MeOH, c =1.2); UV λ max nm 281 (log ε 3.94); IR ν_{max} cm^{-1} 3450, 1680, 1660, 1610. CIMS *m/z* 659 $(MH)^+$. ^1H and ^{13}C NMR see Table 4.

CRYSTAL DATA. - $C_{37}H_{42}N_2O_9$,1/2 H_2O, M_W = 667.76, crystal of 0.5 x 0.6 x 0.6 mm, tetragonal, space group $P4_32_12$, Z = 8, a = b = 13.214 (5), c = 40.657 (16) Å, V = 7099 (5) $Å^3$, d_{calc} = 1.25 g cm^{-3}, F(000) = 2840, λ (Cu Kα) = 1.5418 Å, μ = 0.70 mm^{-1}. Intensity data were measured on an Enraf-Nonius CAD-4 diffractometer using graphite-monochromated Cu Kα radiation and the (θ-2θ) scan technique up to θ = 65°. Of the 6046 collected reflexions (h: 0-15, k: 0-17, l: 0-47), 5406 were unique (R_{int} = 0.059) and 4795 were considered as observed having $I \geq 3\ \sigma(I)$. The structure was solved by direct methods using *SHELXS86*[14] and refined by block matrix least-squares with *SHELX76*[15], minimizing the function $\Sigma w(Fo-|Fc|)^2$. The hydrogen atoms, located in difference Fourier maps, were introduced at theoretical position [d(C-H) = 1.00 Å] and assigned an isotropic thermal factor equivalent to that of the bonded carbon atom, plus 10 %. Convergence was reached at R = 0.051 and R_w = 0.063 [with $R_w = \{\Sigma w(Fo-|Fc|)^2/\Sigma wFo^2\}^{1/2}$ and $w = 1/[\sigma^2(Fo)+ 0.0004\ Fo^2]$. The residual electron density in the final difference map was located between -0.34 and 0.47 e $Å^3$. A molecule of water, found on a two-fold axis, bridges two molecules of forbesin A through hydrogen bonds (O_{11}..H-O-H.. O_{11} (y,x,2-z) : O...O = 2.885 (3), O...H = 2.02 Å, O..H-O = 158°. An hydrogen bond further links N_{17}-H with O_5 of a neighbouring molecule (1.5 - x, 0.5 + y, 1.75 - z) : N...O = 2.992 (3), H...O = 2.12 Å, N-H..O = 145°. The authors have deposited atomic coordinates, bond lengths, bond and torsion angles, and thermal parameters for the structure at the Cambridge Crystallographic Data Center (UK).

Forbaglin B **(14)**. Amorphous, $[\alpha]_D$ +76° (MeOH, c = 0.2). UV λ max nm 277 (log e 4.26). IR ν_{max} cm^{-1} 3400, 1755, 1671, 1650, 1600. CIMS *m/z* 659 $(MH)^+$. ^1H and ^{13}C NMR see Table 4.

Aglain B acetate **(15)**. Amorphous, $[\alpha]_D$ -76° ($CHCl_3$, c = 0.5) IR ν_{max} cm^1 3445, 1747, 1653, 1622, 1596. CIMS *m/z* 673 $(MH)^+$. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.80 (3H, t, J = 7.5 Hz, H-21), 0.85 (3H, d, J =7 Hz, H-22), 2.45 (3H, s, MeCO), 3.70 (2H, s, MeO-4'), 3.72, 3.75 (2 x 3H, 2s, MeO-6, MeO-8), 4.13 (1H, d, J = 10 Hz, H-3), 4.60 (1H, d, J = 10 Hz, H-4), 5.18, (1H, d, J = 8 Hz, NH), 5.68 (1H, s, H-10), 6.05 (1H, d, J = 2 Hz, H-7), 6.07 (1H, d, J = 2 Hz, H-9), 6.62 (2H, d, J = 9 Hz, H-3'5), 7.05 (2H, d, J = 9 Hz, H-2'6'), 7.10 (5H, m, H-2"6", H-3"5", H-4"). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 11.7 (C-21), 16.8 (C-22), 21.4 (C-15, MeCO), 26.3 (C-20), 34.3 (C-14), 42.0 (C-19), 46.0 (C-16), 55.2, 55.4, 56.0 (MeO-6, MeO-8, MeO-4'), 63.3 (C-4), 63.5 (C-13), 79.6 (C-10), 81.6 (C-5), 88.2 (C-2), 92.5 (C-7), 94.6 (C-9), 105.0 (C-5a), 113.2 (C-3'5'), 126.2 (C-4'), 128.2 (C-3"5"), 129.0 (C-1'), 130.0 (C-2'6', C-2"6"), 141.7 (C-1"), 153.4 (C-1a), 157.8 (C-6), 159.0 (C-4'), 161.3 (C-8), 169.0 (C-11), 170.6 (COMe), 174.8 (C-18).

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7. Odorine **5** was a mixture of two isomers (2R, 2'S and 2S, 2'S)[16]. **5** has also been isolated from an ethanol extract of the leaves of *A. forbesii*.
8. Apotirucallanes triterpenes and cycloartanes were also isolated from *Aglaia argentea* (bark and leaves respectively) and have been described previously[12,13].
9. This work has been done in the framework of a collaborative program between CNRS (France) and the University of Malaya (Kuala Lumpur, Malaysia).
10. Relative configuration as depicted in **7-11**, **14** or **15.**
11. A S-configuration is shown at C-19, which is the same as previously found for the corresponding carbon of odorine[7].
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