Chemical Constituents of the Flowers of *Azadirachta indica*

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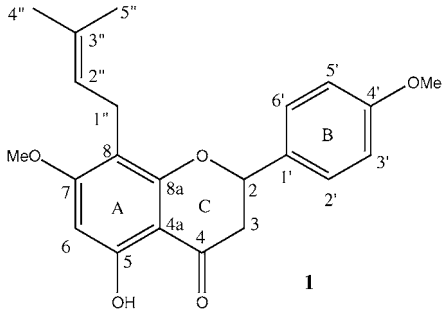
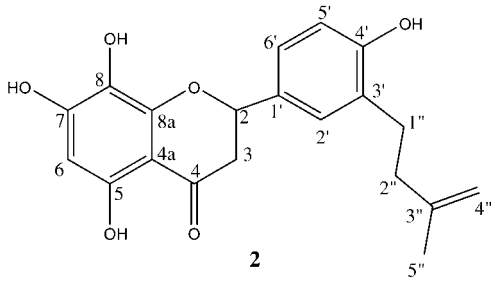
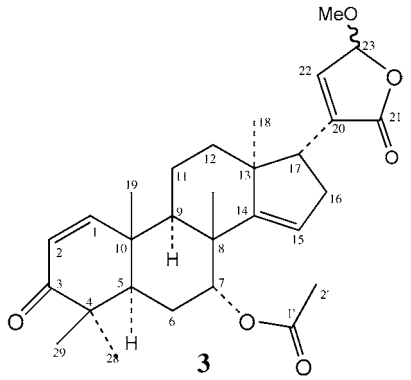
Studies on the chemical constituents of the flowers of *Azadirachta indica* have led to the isolation of two new flavanones, flowerine (= 5-hydroxy-7,4′-dimethoxy-8-(3-methylbut-2-enyl)flavan-4-one; **1**) and flowerone (= 5,7,8,4′-tetrahydroxy-3′-(3-methylbut-3-enyl)flavan-4-one; **2**), and two new triterpenoids, *O*-methylazadironolide (= 7α-(acetoxy)-23ξ-methoxy-21,23-epoxy-24,25,26,27-tetranorapotirucalla-1,14,20(22)-trien-3,21-dione; **3**) and diepoxyazadirol (= (20*S*,23*S*,24*R*)-7-α-(acetoxy)-25-hydroxy-21,24 : 23,24-diepoxyapotirucalla-1,14-dien-3-one; **4**) along with the known triterpenoid trichilenone acetate (= 7α-(acetoxy)-14,15 : 21,23-diepoxy-24,25,26,27-tetranorapotirucalla-1,20,22-trien-3-one; **5**), two known flavanones, nimbaflavone (= 5,7-dihydroxy-4′-methoxy-8,3′-bis(3-methylbut-2-enyl)-flavan-4-one; **6**) and 3′-prenylnaringenin (= 5,7,4′-trihydroxy-3′-(3-methylbut-2-enyl) flavan-4-one; **7**), and 4-(2-hydroxyethyl)phenol (**8**). Their structures have been elucidated through spectral studies, including 2D-NMR experiments, and chemical transformation. Compounds **5**, **7** and **8** are heretofore unreported from any part of tree, while **6** has been isolated earlier from leaves.

1. Introduction. – Various parts of A*zadirachta indica* A. Juss. (syn. *Melia azadirachta* Linn.), a member of family Meliaceae, are highly reputed for the treatment of several human ailments, particularly for diseases of bacterial and fungal origin. Its leaves have been used in ulcer, eczema, jaundice, and liver complaints, whereas its fruits are considered purgative and emollient, useful in the treatment of intestinal worm, urinary diseases, and piles. The bark is a bitter tonic, astringent, and anti-periodontic, and dried flowers are considered tonic and stomachic [1][2]. Although the different parts have been studied extensively for their chemical constituents [3–14], systematic studies on the flowers have been lacking. Hence, the present studies undertaken on the fresh flowers of *A. indica* have resulted in the isolation and structure elucidation of four new and four known constituents. These include two new flavanones, flowerine (**1**) flowerone (**2**), two new triterpenoids, *O*-methylazadironolide (**3**) and diepoxyazadirol (**4**), the known triterpenoid trichilenone acetate (**5**) [15], two known flavanones, nimbaflavone (**6**) [16] and 3′-prenylnaringenin (**7**) [17], and a phenolic constituent, 4-(2-hydroxyethyl)phenol (**8**) [18]. Flavanone **6** was reported earlier from the leaves of *A. indica* [16], but its presence in the flowers is hitherto unreported. Compounds **5**, **7**, and **8** are, until now, unreported from any part of the tree. The assignments for the ^{13}C-nuclei of **5** are reported for the first time.

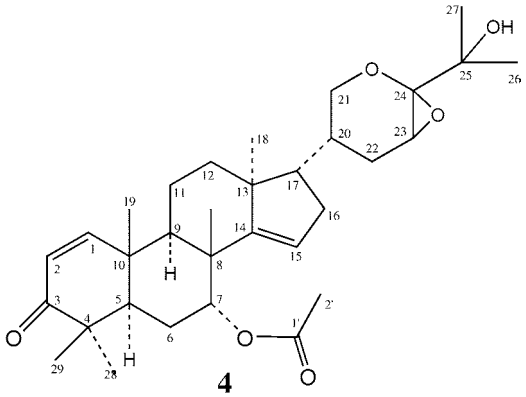
2. Results and Discussion. – The molecular formula of flowerine (**1**) was established as $C_{22}H_{24}O_5$ by the M^+ ion at *m/z* 368.1620 in the HR-EI-MS. The UV spectrum showed an absorption maximum at 292.6 nm (log ε 4.16), which, along with eleven degrees of unsaturation in the molecule, indicated an aromatic system.







In the ^{1}H-NMR spectrum, a pair of *AB d* at δ 7.34 (H–C(2′), H–C(6′)) and δ 6.91 (H–C(3′), H–C(5′)) with $J(3',5') = 8.7$ suggest a *para* substituted aromatic ring, while a 1-H *s* at δ 6.07 (H–C(6)) indicates a second aromatic system. Two aromatic spin systems are also evident from the ^{13}C-NMR spectrum (*Table 1*). Further, two *s* at δ 3.81 and 3.83, each integrating as three protons, indicate the presence of two MeO groups, while a signal at δ 12.11 can be assigned to a H-bonded OH proton. The presence of an isoprenyl unit is indicated by typical chemical shifts and *J* values (*Table 1*) [17]. Further, two *dd* were observed at δ 3.07 (H_{ax}–C(3′)) with $J(3_{ax},3_{eq}) = 17.1$, $J(2,3_{ax}) = 12.6$; and δ 2.82 (H_{eq}–C(3)) with $J(3_{ax},3_{eq}) = 17.1$, $J(2,3_{eq}) = 3.0$; along with a *dd* at δ 5.35 (H–C(2)) with $J(2,3_{ax}) = 12.6$; $J(2,3_{eq}) = 3.0$, which indicate that C(2) is substituted. These spectral features indicate that **1** is a flavonoid with an aromatic ring containing only one H-atom and another ring substituted at the *para*-position [19]. The substitution pattern of **1** was further supported by mass fragments at *m/z* 234.0895 ($C_{13}H_{14}O_4^+$) and at *m/z* 134.0738 ($C_9H_{10}O^+$) resulting from *retro-Diels–Alder* fragmentation around ring C. Further fragmentation of the ion $C_{13}H_{14}O_4^+$ furnished a fragment at *m/z* 179.0340 ($C_9H_7O_4^+$). In the HMBC



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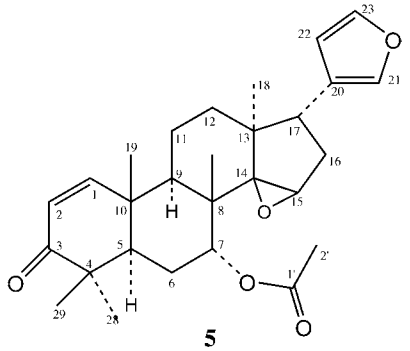

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spectrum, H–C(6′) (δ 7.34) and H–C(2′) (δ 7.34) showed long-range connectivity with C(4′) (δ 159.8) and C(2) (δ 78.5). H–C(1″) (δ 3.20) had connectivity with C(3″) (δ 131.3), C(2″) (δ 122.4), C(7) (δ 165.7), C(8) (δ 108.9), and C(8a) (δ 158.9); H–C(6) (δ 6.07) had connectivity with C(5) (δ 162.6), C(4a) (δ 102.9), C(7) (δ 165.7), and C(8) (δ 108.9); H_{ax}–C(3) (δ 3.07) and H_{eq}–C(3) (δ 2.82) showed connectivity with C(2) (δ 78.5) and C(4) (δ 196.5); one of the MeO groups (δ 3.81) showed connectivity with C(4′) (δ 159.8), while the second MeO group (δ 3.83) showed connectivity with C(7) (δ 165.7) and were, therefore, placed at C(4′) and C(7) respectively.

These connectivities further show that the isoprenyl unit is at C(8), and the OH group is at C(5), H-bonded to the C(4)=O group. In the light of these observations, the structure of **1** has been elucidated as 5-hydroxy-7,4′-dimethoxy-8-(3-methylbut-2-enyl)flavan-4-one.

The molecular formula of **2** was found to be $C_{20}H_{20}O_6$ by M^+ ion in the HR-EI-MS at *m/z* 356.1260. The UV spectrum displays a maximum at 290.0 nm (log ε 3.83), and eleven degrees of unsaturation in the molecule indicated an aromatic system.

In the ^{1}H-NMR spectrum, a *dd* appearing at δ 7.03 (H–C(6′)), a *d* at δ 6.72 (H–C(5′)), and a br. *s* at δ 6.97 (H–C(2′)) suggest *ortho-ortho* and *ortho-meta* coupled systems in an aromatic ring, while a 1-H *s* at δ 5.77 (H–C(6)) indicates the presence of another aromatic system bearing only H-atom [16]. These were also evident from ^{13}C-NMR data (*Table 1*). A H-bonded OH signal appeared at δ 12.04. Further, two *dd* at δ 2.96 (H_{ax}–C(3)) with $J(3_{ax},3_{eq})=17.0$, $J(2,3_{ax})=13.0$, and δ 2.57 (H_{eq}–C(3)) with $J(3_{ax},3_{eq})=17.0$, $J(2,3_{eq})=3.0$;

Table 1. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$) *of the Flavanones* **1** *and* **2**. δ in ppm, J in Hz.

	1		**2**	
	δ(H)[a])	δ(C[b])	δ(H)[c])	δ(C)[d])
H–C(2)	5.35 (*dd*, *J* = 12.6, 3.0)	78.5	5.15 (*dd*, *J* = 13.0, 3.0)	78.9
H_{ax}–C(3)	3.07 (*dd*, *J* = 17.1, 12.6)	43.3	2.96 (*dd*, *J* = 17.0, 13.0)	42.9
H_{eq}–C(3)	2.82 (*dd*, *J* = 17.1, 3.0)		2.57 (*dd*, *J* = 17.0, 3.0)	
C(4)	–	196.5	–	196.1
C(5)	–	162.6	–	163.1
H–C(6)	6.07 (*s*)	92.4	5.77 (*s*)	95.4
C(7)	–	165.7	–	155.9
C(8)	–	108.9	–	129.5
C(4a)	–	102.9	–	102.1
C(8a)	–	158.9	–	151.9
C(1′)	–	130.9	–	129.5
H–C(2′)	7.34 (*d*, *J* = 8.7)	127.5	6.97 (br. *s*)	129.4
H–C(3′)	6.91 (*d*, *J* = 8.7)	114.0	–	126.1
C(4′)	–	159.8	–	155.9
H–C(5′)	6.91 (*d*, *J* = 8.7)	114.0	6.72 (*d*, *J* = 8.3)	116.4
H–C(6′)	7.34 (*d*, *J* = 8.7)	127.5	7.03 (*dd*, *J* = 8.3, 2.3)	126.0
H–C(1″)	3.20 (*d*, *J* = 7.2)	21.6	2.14 (*t*, 7.5)	31.6
H_a–C(2″)	5.13 (*t*, *J* = 7.2)	122.4	2.80 (*dd*, *J* = 14.0, 7.5)	38.4
H_b–C(2″)	–	–	2.68 (*dt*, *J* = 14.0, 2.9)	
C(3″)	–	131.3	–	146.1
H_a–C(4″)	1.59 (*s*)	25.8	4.79 (*s*)	110.5
H_b–C(4″)	–		4.64 (*s*)	
H–C(5″)	1.63 (*s*)	17.7	1.61 (*s*)	17.7
MeO	3.83 (*s*)	55.8	–	–
MeO	3.81 (*s*)	55.3	–	–
HO–C(5)	12.11 (*s*)	–	12.04 (*s*)	–

[a]) Recorded at 400 MHz. [b]) Recorded at 75 MHz. [c]) Recorded at 500 MHz. [d]) Recorded at 100 MHz.

along with a *dd* at δ 5.15 (H–C(2)) with $J(2,3_{ax}) = 13.0$, $J(2,3_{eq}) = 3.0$, indicate a flavanone nucleus. The presence of a 3-methylbut-3-ene unit is indicated by characteristic δ (H)s and J values (*Table 1*) [20]. These features manifest three substitutions in ring A and two substitutions in ring B located at C(2). The HMBC spectrum shows long-range connectivity of H–C(6′) (δ 7.03) with C(4′) (δ 155.9), C(2′) (δ 129.4), and C(2) (δ 78.9); H–C(5′) (δ 6.72) with C(2′) (δ 129.4) and C(3′) (δ 126.1); H–C(2′) (δ 6.97) with C(3′) (δ 126.1) and C(4′) (δ 155.9); and H–C(1″) (δ 3.20) with C(1′) (δ 129.5), C(2′) (δ 129.4), and C(3′) (δ 126.1).

In the light of these observations, the structure of **2** has been elucidated as 5,7,8,4′-tetrahydroxy-3′-(3-methylbut-3-enyl)flavan-4-one, which obtained additional support from mass fragments at *m/z* 188.1205 ($C_{13}H_{16}O^+$) and 168.0103 ($C_7H_4O_5^+$) resulting from *retro-Diels–Alder* fragmentation in ring-C.

HR-EI-MS of **3** shows an M^+ peak at *m/z* 482.2665, corresponding to the molecular formula $C_{29}H_{38}O_6$. Its triterpenoidal nature is indicated by the presence of five quaternary Me *s* at δ 0.87, 1.18, 1.06 (two *s*), and 1.21 in the ^{1}H-NMR spectrum, which were assigned to the Me(18, 19, 28, 29, and 30) respectively. *A* pair of *AB d* at δ 7.12 and 5.83 (H–C(1) and (H–C(2), respectively) with $J(1,2) = 10.2$, and mass fragments at *m/z* 137.0969 ($C_9H_{13}O^+$) and 150.1047 ($C_{10}H_{14}O^+$) in the HR-EI-MS indicate a 1-en-3-one system in ring A. A typical pair of *dd* resonating at δ 2.17 (H–C(5)) with $J(5,6_\alpha) = 12.8$, $J(5,6_\beta) = 2.9$, and at δ 2.28 (H–C(9)) with $J(9,10_\beta) = 11.5$, $J(9,10_\alpha) = 2.8$ are attributable to H–C(5) and H–C(9), respectively. A *s* at δ 1.94 indicates the presence of the AcO group at C(7) and a narrow *m* resonating at δ 5.24 is due to H_{eq}–C(7). The ^{1}H-NMR spectrum further

shows a *m* attributed to H–C(15) at δ 5.34. These spectral data and the mass fragment at *m/z* 368.2357 ($C_{24}H_{32}O_3^+$) clearly show that the tetracyclic skeleton of **3** is identical to that of azadirone [9][13]. Thus, a $C_5H_5O_3$ unit was left to be decided. The signals typical for a furan ring were absent and, instead, two 1-H *s* at δ 5.74 (H–C(23)) and δ 6.85 (H–C(22)) were observed, which shows the presence of a γ-hydroxybutenolide ring [13]. A *s* of three H-atoms at δ 3.56 was due to MeO group in the side chain at C(23).

These observations led us to deduce the structure of **3** as 7α-(acetyloxy)-23ξ-methoxy-21,23-epoxy-24,25,26,27-tet ranorapotirucalla-1,14,20(22)-trien-3,21-dione[1]). Thus, **3** can be considered the methyl derivative of azadironolide [13], and this is the first instance of its isolation as a natural product. The spectral data of **3** (*Table 2*) match well those of *O*-methylazadironolide prepared from an authentic sample [13].

The molecular formula of **4** was established as $C_{32}H_{46}O_6$ by an ion in the HR-EI-MS at *m/z* 526.3274. The MS fragments at *m/z* 137.0969 ($C_9H_{13}O^+$), 150.1047 ($C_{10}H_{14}O^+$), and 368.2357 ($C_{24}H_{32}O_3^+$) in the MS and the NMR data (*Tables 2* and *3*) clearly show that the rings A–D of **4** are identical to those of **3** and azadirone [9][13].

The ^{1}H-NMR spectrum further shows three *dd* sets at δ 3.86 (H–C(23)), 3.81 (H_a–C(21)) and 3.61 (H_b–C(21)) showing the presence of oxygenated C-atoms, as also indicated by the transmissions characteristic for C–O bonds in the IR spectrum (*vide Exper. Part*). In the HMBC spectrum, these H-atoms show connectivity with the anomeric quaternary C(24) resonating at δ 95.9. In the HMQC spectrum, the H–C(23) proton has connectivity with the C(23) (δ 67.5) and both H_a–C(21) and H_b–C(21) with C(21) (δ 65.4). The ^{1}H-NMR spectrum shows two 3-H *s* at δ 1.25 and 1.40 besides the *s* for Me groups located in tetracyclic nucleus. The HMBC spectrum shows connectivity of these Me groups with C(24) and C(25) (δ 76.3). The chemical shifts and HMBC correlations of these Me H-atoms with C(24) and C(25) show the presence of a OH group at C(25). These features led us to formulate a pyran ring with an epoxy ring bridging C(23) and C(24) and a Me_3COH moiety at C(24) in the side chain. The epoxide is oriented on the β-side. H–(23), appearing as a *dd* with $J(23_{ax},22_{ax}) = 9.0$ and $J(23_{ax},23_{eq}) = 3.0$ [21]. In the NOESY plot, H–C(20) (δ 1.24) showed interaction with H_α–C(18) (δ 1.05), which showed that the side chain is oriented on the α-side. Thus, **4** was assigned the structure as (20*S*,23*S*,24*R*)-7α-(acetyloxy)-21,24 : 23,24-diepoxyapotirucalla-1,14-dien-3-one.

Treatment of **4** with Ac_2O/pyridine afforded derivative **4a**: the molecular formula $C_{36}H_{52}O_9$ was established on the basis of the molecular-ion peak in the HR-EI-MS at *m/z* 628.3618, which showed the incorporation of a whole molecule of Ac_2O. The mass fragments at *m/z* 137.0969 ($C_9H_{13}O^+$), 150.1047 ($C_{10}H_{14}O^+$), and 368.2357 ($C_{24}H_{32}O_3^+$) and the ^{1}H- and ^{13}C-NMR data show that the basic skeleton had remained intact. However, in the ^{1}H-NMR spectrum two additional *s* for acetyl H-atoms are present at δ 2.06 and 2.07 besides the C(7) Ac group at δ 1.94. Moreover, the signals for H–C(21), H–C(23) were shifted downfield in the ^{1}H-NMR spectrum, and a marked change from δ 95.9 to δ 210.9 was observed in the chemical shift of C(24), suggesting the presence of a carbonyl group at C(24). These data suggest opening of the pyran ring of **4** during reaction with Ac_2O/pyridine and acetylation at both C(21) and C(23) (*Scheme*). The spectral data of **4a** is analogous to that of diacetylazadirol, the Ac derivative of azadirol isolated earlier from the fruit coats of *A. indica* [22]. The isolation of **4** suggests that the previously reported compound azadirol may be formed as an artifact by opening of the pyran ring during isolation.

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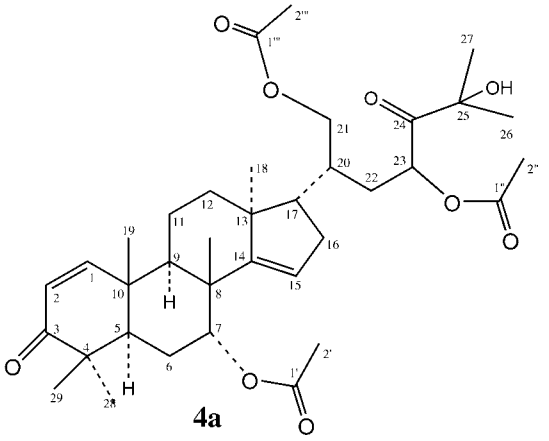
[1]) The parent triterpenoid tirucallane is identical to the parent euphane except for configuration at C(20). The systematic names of tirucallane and euphane are (13α,14β,17α,20*S*)- and (13α,14β,17α,20*R*)-lanostane, respectively. The prefix apo indicates migration of the 14β-Me group to the 8β-position. Thus, **3**–**5** may also be named as euphane derivatives.

Table 2. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$) *of the Triterpenes* **3** *and* **5**. δ in ppm, J in Hz.

	3		**5**	
	δ(H)[a])	δ(C)[b])	δ(H)[c])	δ(C)[b])
H–C(1)	7.12 (*d*, *J* = 10.2)	158.1	7.18 (*d*, *J* = 10.2)	158.4
H–C(2)	5.83 (*d*, *J* = 10.2)	125.1	5.85 (*d*, *J* = 10.2)	125.5
C(3)	–	203.8	–	204.6
C(4)	–	45.3	–	44.3
H–C(5)	2.17 (*dd*, *J* = 12.8, 2.9)	46.6	2.17 (*dd*, *J* = 13.1, 2.9)	46.7
H_α–C(6)	1.88 (*m*)	23.9	1.88 (*ddd*, *J* = 15.0, 2.3, 2.9)	24.4
H_β–C(6)	1.76 (*m*)	–	1.76 (*ddd*, *J* = 15.0, 13.0, 2.3)	–
H–C(7)	5.24 (*m*)	72.0	4.73 (*t*, 2.3)	74.0
C(8)	–	42.8	–	42.7
H–C(9)	2.28 (*dd*, *J* = 11.5, 2.8)	38.6	2.55 (*ddd*, *J* = 12.0, 4.8)	40.4
C(10)	–	41.1	–	39.8
H_α–C(11)	1.90 (*m*)	16.3	1.90 (*m*)	16.3
H_β–C(11)	1.78 (*m*)	–	1.78 (*m*)	–
H_α–C(12)	1.80 (*m*)	34.0	1.80 (*m*)	29.6
H_β–C(12)	1.90 (*m*)	–	1.90 (*m*)	–
C(13)	–	46.9	–	42.0
C(14)	–	157.6	–	73.2
H–C(15)	5.34 (*m*)	119.6	3.41 (br. *s*)	57.4
H_α–C(16)	2.51 (*m*)	34.9	1.60 (*m*)	32.2
H_β–C(16)	2.31 (*m*)	–	2.13 (*m*)	–
–				
H–C(17)	2.15 (*m*)	54.4	2.62 (*dd*, *J* = 11.0, 6.1)	39.6
Me(18)	0.87 (*s*)	20.0	0.94 (*s*)	21.9
Me(19)	1.18 (*s*)	19.0	1.11 (*s*)	19.4
C(20)	–	158.7	–	123.8
H–C(21)	–	169.7	7.08 (*dd*, *J* = 2.4, 1.2)	139.5
H–C(22)	6.85 (br. *s*)	119.2	6.14 (*dd*, *J* = 1.8, 1.2)	111.0
H–C(23)	5.74 (br. *s*)	97.4	7.34 (*t*, 3.4)	142.9
Me(28)	1.06 (*s*)	21.3	1.05 (*s*)	19.9
Me(29)	1.06 (*s*)	27.1	1.05 (*s*)	21.4
Me(30)	1.21 (*s*)	29.7	1.18 (*s*)	27.1
C(1′)	–	170.0	–	169.9
Me(2′)	1.94 (*s*)	21.1	2.04 (*s*)	21.1
MeO	3.56 (*s*)	55.9	–	–

[a]) Recorded at 500 MHz. [b]) Recorded at 100 MHz. [c]) Recorded at 400 MHz.



4a

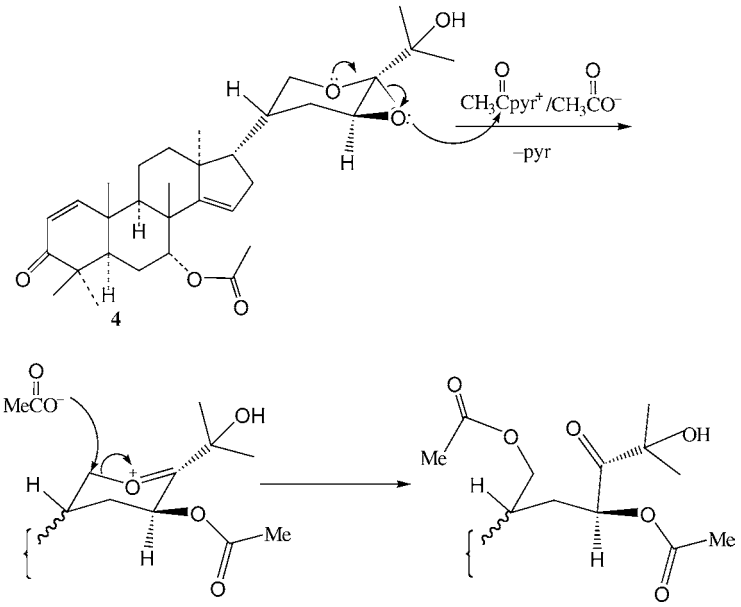
Table 3. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$) *of the Triterpenes* **4** *and* **4a**. δ in ppm, J in Hz.

	4		**4a**	
	δ(H)[a])	δ(C)[b])	δ(H)[a])	δ(C)[b])
H–C(1)	7.13 (*d*, *J* = 10.2)	158.1	7.13 (*d*, *J* = 10.5)	158.0
H–C(2)	5.83 (*d*, *J* = 10.2)	125.5	5.85 (*d*, *J* = 10.5)	125.6
C(3)	–	204.6	–	204.6
C(4)	–	44.1	–	44.1
H–C(5)	2.18 (*dd*, *J* = 12.8, 2.9)	46.2	2.20 (*m*)	46.2
H_α–C(6)	1.94 (*m*)	23.8	1.95 (*dd*, *J* = 12.3, 3.5)	23.8
H_β–C(6)	1.76 (*m*)	–	1.74 (*m*)	–
H–C(7)	5.20 (*m*)	74.6	5.22 (*t*, 3.5)	74.6
C(8)	–	42.8	–	42.8
H–C(9)	2.21 (*dd*, *J* = 11.7, 4.2)	38.5	2.25 (*dd*, *J* = 11.7, 4.2)	38.9
C(10)	–	39.8	–	39.8
H_α–C(11)	1.95 (*m*)	16.7	1.94 (*m*)	16.7
H_β–C(11)	1.60 (*m*)	–	1.63 (*m*)	–
H_α–C(12)	1.78 (*m*)	33.9	1.78 (*m*)	34.8
H_β–C(12)	1.65 (*m*)	–	1.65 (*m*)	–
C(13)	–	45.8	–	46.2
C(14)	–	158.7	–	159.1
H–C(15)	5.31 (*m*)	119.2	5.30 (*m*)	119.1
H_α–C(16)	2.14 (*m*)	34.5	2.03 (*ddd*, *J* = 15.1, 11.1, 3.4)	34.0
H_β–C(16)	1.91 (*m*)	–	1.91 (*ddd*, *J* = 15.1, 7.2, 3.7)	–
H–C(17)	3.36 (*m*)	57.6	1.80 (*m*)	55.4
Me(18)	1.05 (*s*)	21.3	1.01 (*s*)	21.1
Me(19)	1.15 (*s*)	20.0	1.16 (*s*)	20.5
H–C(20)	1.24 (*dd*, *J* = 7.5, 2.8)	29.8	2.06 (*s*)	36.6
H_α–C(21)	3.81 (*dd*, *J* = 11.5, 3.0)	65.4	4.29 (*dd*, *J* = 11.5, 3.2)	65.4
H_β–C(21)	3.61 (*dd*, *J* = 11.5, 5.0)	–	3.97 (*dd*, *J* = 11.5, 5.3)	–
H_α–C(22)	1.96 (*m*)	34.9	1.92 (*dt*, 15.3, 2.8, 2.8)	31.2
H_β–C(22)		–	1.781.96 (*m*)	–
H–C(23)	3.86 (*dd*, *J* = 10.0, 4.0)	67.5	5.61 (*dd*, *J* = 9.0, 3.0)	67.5
C(24)	–	95.9	–	210.9
C(25)	–	76.3	–	76.6
Me(26)	1.25 (*s*)	23.1	1.38 (*s*)	27.7
Me(27)	1.40 (*s*)	24.4	1.42 (*s*)	27.4
Me(28)	1.06 (*s*)	21.3	1.05 (*s*)	20.9
Me(29)	1.06 (*s*)	27.1	1.06 (*s*)	27.0
Me(30)	1.21 (*s*)	27.4	1.14 (*s*)	25.9
C(1′)	–	170.0	–	170.0
H–C(2′)	1.92 (*s*)	21.2	1.94 (*s*)	21.1
C(1″)	–	–	–	171.8
H–C(2″)	–	–	2.06 (*s*)	19.0
C(1‴)	–	–	–	169.6
H–C(2‴)	–	–	2.07 (*s*)	19.6
HO–C(25)	3.34 (*s*)	–	3.36 (*s*)	–

[a]) Recorded at 500 MHz. [b]) Recorded at 100 MHz.

The formation of **4a** is envisaged to occur by the attack of epoxide O-atom on the Ac C=O group facilitated by the pushing effect of the pyran ring O-atom, resulting in epoxide ring opening with retention of configuration, followed by the attack of AcO group on C(21).

Scheme



Experimental Part

General. Column chromatography (CC) and flash chromatography (FC): silica gel *9385* (*Merck*, 0.040–0.063 mm). Prep. TLC: silica gel *60 PF_{254}* (*Merck*); detection with I_2 spray. UV Spectra (MeOH): *Hitachi U-3200* spectrophotometer; λ_{max} (log ε) in nm. IR Spectra ($CHCl_3$): *Jasco A-302* spectrophotometer; ν in cm^{-1}. ^{1}H-NMR, COSY, NOESY, and *J*-resolved: *Bruker AM-400* and *AMX-500* spectrometers; chemical shifts δ in ppm. rel. to $SiMe_4$ as internal standard, coupling constants *J* in Hz. ^{13}C-NMR: *Bruker* spectrometer at 75 and 100 MHz. EI-MS: *Finnigan-Mat 311A* mass spectrometer; source at 250° and 70 eV; *m/z* (rel.-%). HR-EI-MS: *Jeol JMS-HX-110* mass spectrometer; EI, source at 250° and 70 eV; *m/z* (rel.-%). Hexane was of boiling range 60–80°.

Plant Material. The fresh flowers of *A. indica* were collected from Karachi region during April 1999 and were identified by Prof. Dr. *S. I. Ali*, Department of Botany, University of Karachi, and a voucher specimen (No. NM-1) has been deposited in the Herbarium of the Department of Botany, University of Karachi, Karachi.

Extraction and Isolation. The fresh flowers (4 kg) of *A. indica* were extracted repeatedly (4 ×) with MeOH at r.t. The combined extract was concentrated under vacuum and divided into neutral (NF) and acidic (AF) fractions by treatment with 4% aq. Na_2CO_3. The NF was further divided into hexane soluble (NFHS) and insoluble (NFHI) fractions after treatment with activated charcoal. The latter (NFHI) was again divided into hexane/ether 1:1 soluble (NFHIES) and insoluble (NFHIEI) fractions. The NFHIES fraction (2.5 g) was subjected to gravity CC (hexane → hexane/AcOEt 9:1 to 7:3 → $CHCl_3$, $CHCl_3$/MeOH → MeOH). As a result, 60 fractions were obtained and combined on the basis of TLC to ultimately afford eight fractions (A–H). Fraction B (35 mg), purified by prep. TLC ($CHCl_3$/MeOH; 9.7:0.3) furnished **1** as an amorphous powder (3.3 mg). The NFHIEI fraction (4.8 g) was also subjected to gravity CC (hexane → hexane/AcOEt 9:1 to 7:3 → $CHCl_3$ → $CHCl_3$/MeOH). As a result, 61 fractions were obtained and combined on the basis of TLC to ultimately afford seven fractions (*A′–G′*). *Fr. A′* (354 mg) was again subjected to CC (hexane, hexane/AcOEt 9.5:0.5 to 7:3, in order of increasing polarity). As a result, five fractions (*A1′–A5′*) were obtained, after combining various fractions on the basis of TLC. *Fr. A2′* on purification through prep. TLC ($CHCl_3$/MeOH; 9.7:0.3) furnished **3** as an amorphous powder (9 mg). *Fr. C′* (560 mg), was again subjected to CC (hexane → hexane/AcOEt 9.5:0.5 to 7:3) resulting in four fractions (*C1′–C4′*). Of these, *Fr. C3′* was purified by prep. TLC (hexane/AcOEt 6:4) to furnish **4** as an amorphous powder (10.5 mg). *Fr. D′* (422.6 mg) was also subjected to

CC, ($CHCl_3 \rightarrow CHCl_3$/MeOH) to afford three fractions (*D1′ – D3′*), from which *Fr. D1′* on purification by prep. TLC (hexane/AcOEt; 6.5 : 3.5) provided **7** [17] as an amorphous powder (8 mg) *Fr D2′* by prep. TLC (hexane/AcOEt; 6 : 4) furnished **2** as amorphous powder (4.4 mg). *Fr. E′* (368.8 mg) on CC ($CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH) afforded two fractions (*E1′* and *E2′*); of these fraction, *E1′* (124.1 mg) was purified by prep. TLC (CH_2Cl_2/MeOH; 9.7 : 0.3), furnishing **8** [18] as an amorphous powder (28.0 mg).

In another workup, the fresh flowers (2 kg) of *A. indica* were extracted repeatedly (4 ×) with hexane at r.t. The extract was concentrated under vacuum and partitioned between hexane and 90% aq. MeOH. The 90% MeOH phase was extracted with AcOEt after saturation with saline. The AcOEt layer on usual workup and removal of the solvent under vacuum furnished a semi-solid residue (3.61 g), which was subjected to FC and eluted with hexane → hexane/AcOEt 9 : 1 to 7 : 3 → $CHCl_3$ → $CHCl_3$/MeOH. As a result, 63 fractions were obtained, which were combined on the basis of TLC to ultimately afford 18 fractions (*2A – 2R*). *Fr. 2E* on purification through prep. TLC (hexane/AcOEt; 9 : 1) furnished **5** [15], as an amorphous powder (7 mg). *Fr. 2 H* (18 mg), on purification by prep. TLC (hexane/AcOEt 8 : 2), furnished **6** [16] as needle-like crystals (5 mg).

Acetylation of **4**: Compound **4** (10.5 mg) was treated with Ac_2O (0.5 ml) in the presence of pyridine (0.5 ml) and left overnight at r.t., and worked up with H_2O and AcOEt. The AcOEt phase was dried (Na_2SO_4), concentrated under vacuum, purified through prep. TLC (hexane/AcOEt 6 : 4) to afforded *diacetyl azadirol* (**4a**) as amorphous powder (1.5 mg).

Flowerine (*= 5-Hydroxy-7,4′-dimethoxy-8-(3-methyl-2-enyl)flavan-4-one*; **1**): Amorphous powder. UV (MeOH): 292.6 (4.16), 329.4 (3.62), 336.0 (3.62). IR ($CHCl_3$): 3406, 2924, 2854, 1635, 1587, 1516, 1445, 1373, 1252, 1173, 1103. ^{1}H- and ^{13}C-NMR: *Table 1*. HR-EI-MS: 368.1620 (13, $C_{22}H_{24}O_5$, M^+), 234.0895 (10, $C_{13}H_{14}O_4$), 134.0738 (18, $C_9H_{10}O$), 179.0340 (41, $C_9H_7O_4$), 69.0704 (100, C_5H_9).

Flowerone (*= 5,7,8,4′-Tetrahydroxy-3′-(3-methyl-but-3-enyl)flavan-4-one*; **2**): Amorphous powder. UV (MeOH): 290.0 (3.83), 260.4 (3.48). IR ($CHCl_3$) 3366, 2923, 2853, 1639, 1601, 1540, 1506, 1458, 1374, 1342. ^{1}H- and ^{13}C-NMR: *Table 1*. HR-EI-MS: 356.1260 (13, $C_{20}H_{20}O_6$, M^+), 286.0475 (100, $C_{15}H_{10}O_6$), 188.1205 (5, $C_{13}H_{16}O$), 168.0103 (5, $C_7H_4O_5$), 133.0652 (30, C_9H_9O).

O-Methylazadironolide (*= 7α-Acetyloxy)-23ξ-methoxy-21,23-epoxy-24,25,26,27-tetranorapotirucalla-1,14,20(22)-trien-3,23-dione*; **3**): Amorphous powder. UV (MeOH): 205.4. IR ($CHCl_3$): 2900, 2850, 1760, 1720, 1640, 1450, 1375, 1120, 1080, 1015, 930. ^{1}H- and ^{13}C-NMR: *Table 2*. HR-EI-MS: 482.2665 (39, $C_{29}H_{38}O_6$, M^+), 368.2357 (1, $C_{24}H_{32}O_3$), 273.1856 (100, $C_{18}H_{25}O_2$), 150.1047 (71, $C_{10}H_{14}O$), 137.0969 (78, $C_9H_{13}O$).

Diepoxyazadirol (20S,23S,24R)-7α-(acetyloxy-25-hydroxy-)-21,24 :23,24-diepoxyapotirucalla-1,14-d ien-3-one; **4**): Amorphous powder. UV (MeOH): 283.6, 227.2. IR ($CHCl_3$): 3500, 2900, 2850, 1720, 1660, 1450, 1375, 1100, 1120, 1020. ^{1}H- and ^{13}C-NMR: *Table 3*. HR-EI-MS: 526.3274 (2, $C_{32}H_{46}O_6$, M^+), 368.2357 (13, $C_{24}H_{32}O_3$), 150.1047 (71, $C_{10}H_{14}O$), 137.0969 (78, $C_9H_{13}O$), 105.0340 (100, C_7H_5O).

Diacetylazadirol (*= (20S,23S)-7α,21,23-triacetoxy-25-hydroxy-apotirucalla-1,14-dien-3,24-dione*; **4a**): Amorphous powder. UV (MeOH): 283.6, 227.2. IR ($CHCl_3$): 3468, 2929, 2853, 1739.9, 1686, 1445, 1372, 1245, 1030. ^{1}H- and ^{13}C NMR: *Table 3*. HR-EI-MS: 628.3618 (3, $C_{36}H_{52}O_9$, M^+), 368.2357 (100, $C_{24}H_{32}O_3$), 150.1047 (71, $C_{10}H_{14}O$), 137.0969 (78, $C_9H_{13}O$).

Trichilenoneacetate (*= 7α-(acetyloxy)-14,15 :21,23-diepoxy-24,25,26,27-tetranorapotirucalla-1,20,22-trien-3-one*; **5**): Amorphous powder. UV (MeOH): 205.4. IR ($CHCl_3$): 2900, 2850, 1720, 1660, 1450, 1365, 1120, 980. ^{1}H- and ^{13}C-NMR: *Table 2*. HR-EI-MS: 452.2618 (26, $C_{28}H_{37}O_5$, M^+), 368.2352 (13, $C_{24}H_{32}O_3$), 150.1044 (71, $C_{10}H_{14}O$), 137.0965 (100, $C_9H_{13}O$).

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