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A CONVENIENT SYNTHESIS OF FLINDERSINE, ATANINE AND THEIR ANALOGUES

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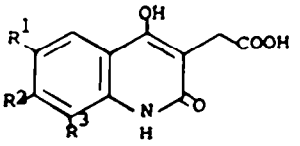
Abstract : A new synthesis of the pyranoquinolone alkaloids flindersine (8a), 8-methoxyflindersine (8c), N-methylflindersine (9a), zanthobunglanine (9c), oricine (9d) and veprisine (9e) and the prenylquinolone alkaloids atanine (13a), preskimmianine (13e), N-methylatanine (14a), O-methylglycosolone (14c) and N-methylpreskimmianine (14e) is described.

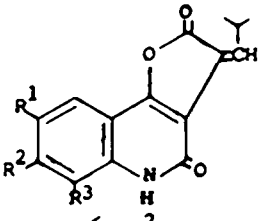
Oxidative cyclisation of 4-hydroxy-3(3-methylbut-2-enyl)-2-quinolones with DDQ constitutes an important method[1] among those[2] hitherto known for the synthesis of pyrano(3,2-c)quinolone alkaloids, as exemplified by the synthesis of flindersine (8a)[1], haplamine (8b)[3], N-methylflindersine (9a)[4,5] and oricine (9d)[5,6]. Though the dehydrocyclisation reaction using DDQ has proved to be a fairly (60-75%) neat one, the overall yield realized of the alkaloids was only 15-16%; the reason being that the method[7] employed for deriving the precursors viz., the prenylquinolones (6) [from diethyl (3-methylbut-2-enyl)malonate and the corresponding aniline] was not quite productive (21-35%) and often attended by unwanted side reactions[8].

It was felt that any methodology that would provide an alternative convenient access to the prenylquinolone precursor or its synthetic equivalent should make the Piozzi's[1] technique more expedient and widely applicable. Recently[9] we have shown how the condensation of isobutyraldehyde with 2-quinolone-3-acetic acids led to a new synthesis of 3(3-methylbut-2-enyl)- as well as 3(3-methylbut-1-enyl)-2-quinolones. The reaction, when applied to 4-hydroxy-2-quinolone-3-acetic acid (1a)[10], gave a mixture of two lactones A (70%) and B (20%), both of which had the same molecular formula $C_{15}H_{13}NO_3$. Compound A (mp. 314-315°) which readily separated from the reaction mixture was collected by filtration and B (mp. 276-277°) was isolated from the filtrate, by extraction with chloroform. Compound B was identified as the linear lactone 3a, on the basis of its ready dissolution in cold aqueous alkali and on its reaction with diazomethane to give the methoxylactone 4a[9]. Compound A, on the other hand, went into solution in aqueous alkali only on heating and did not react with diazomethane and hence presumed to be the angular isomer 2a. 2a as well as 3a gave rise to the same acid 5a, on digestion with hot aqueous alkali followed by acidification. Decarboxylation of 5a furnished a mixture of 6a (24%) and 7a (36%), which were separated by column chromatography and



1

$(CH_3)_2CHCHO$, Ac_2O, AcONa, AcOH

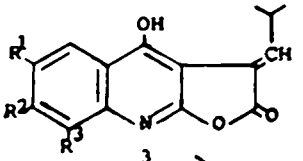


2

CH_2N_2

No reaction

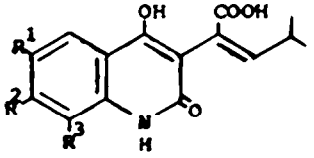
+



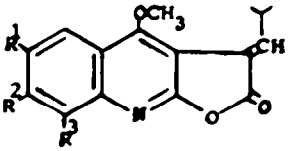
3

1) OH^-
11) H_3O^+

CH_2N_2

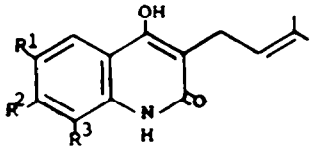


5



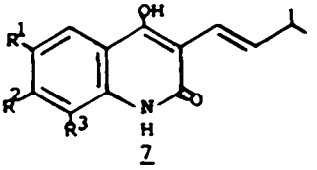
4

Cu / Ph_2O, ∇



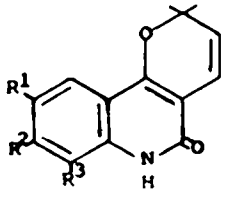
6

+



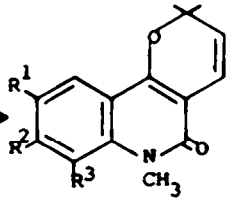
7

DDQ / C_6H_6



8

CH_3I, K_2CO_3

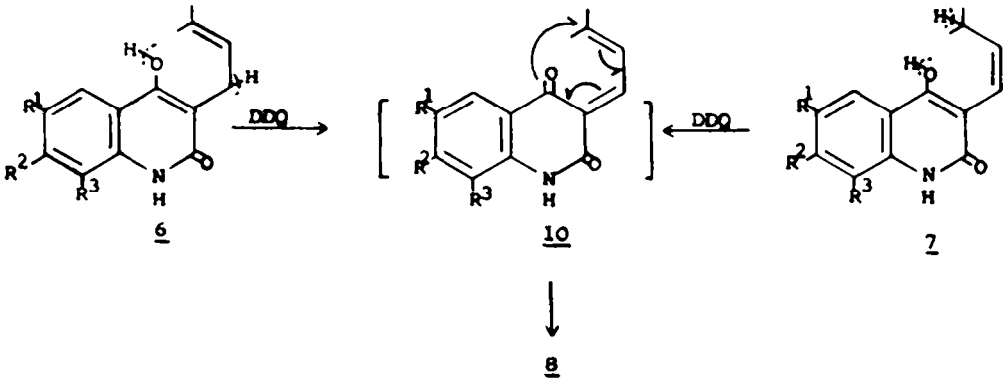


9

	R^1	R^2	R^3
a	H	H	H
b	OCH_3	H	H
c	H	H	OCH_3
d	OCH_3	OCH_3	H
e	H	OCH_3	OCH_3

then characterised. 6a gave flindersine (8a), as reported[1], on heating with DDQ in boiling benzene. Interestingly, the vinyl quinolone 7a also, as expected, gave rise to 8a on dehydrocyclisation with DDQ, thus allowing another access to flindersine (8a)[11]. An improvement (9-11%) in the yield of 8a was realised when the mixture containing 6a and 7a was heated with DDQ without resorting to the process of separating them. On heating with methyl iodide and potassium carbonate in acetone, 8a gave N-methylflindersine (9a)[12], in 75% yield. N-methylderivatives[13] of 6a as well as 7a also yielded 9a on treatment with DDQ in boiling benzene. Extension of the synthetic sequence to the quinolone acids 1c - 1e led to a new synthesis of the alkaloids 8-methoxyflindersine (8c)[14], zanthobunglanine (9c)[15], oricine (9d)[16] and veprisine (9e)[16-18].

The dehydrocyclisation reaction realised with the prenyl- (6) as well as the vinylquinolone (7) can be mechanistically viewed as proceeding through the initial abstraction of the phenolic and the allylic hydrogens to give the quinone-

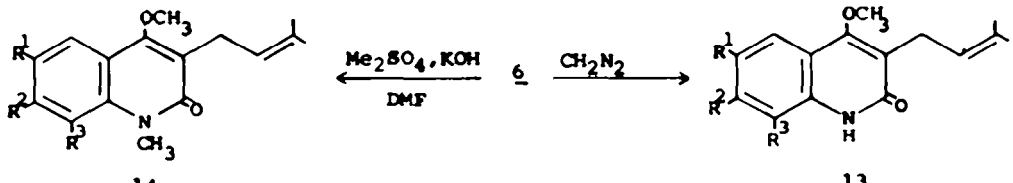


6 10 7

8

methide (10) followed by a pericyclic ring-closure to give the pyranoquinolone (8). A similar mechanism has been established[19] in the DDQ-initiated dehydrocyclisation of 2(3-methylbut-2-enyl)phenol (11) to 2,2-dimethylchromene (12). The intermediacy of the quinone-methide in the transformation of 11 to 12 was further substantiated by their actual isolation[20].

Interestingly, our investigative efforts also provided a convenient



14 13

synthesis of some of the prenylquinolone alkaloids like atanine (13a)[9,21], preskimmianine (13e)[18,22], N-methylatanine (14a)[13,23], O-methylglycosolone (14c)[24] and N-methylpreskimmianine (14e)[18]. Treatment of the prenylquinolones (6) with diazomethane gave the corresponding methylethers (13) whereas with methyl sulphate and alkali in DMF, they afforded the corresponding 4-methoxy-N-methyl-2-quinolones (14).

EXPERIMENTAL

Melting points were determined on a Mettler FP 51 automatic melting point determination apparatus and are uncorrected. The ^{1}H-NMR spectra were recorded on a Hitachi R-600 spectrometer, using TMS as an internal standard. The IR spectra were recorded on a Perkin-Elmer model 597 spectrophotometer.

General Procedure :

Reaction of 1 with isobutyraldehyde : A mixture of 1 (0.02m), isobutyraldehyde (25ml), sodium acetate (4.5g), acetic acid (20ml) and acetic anhydride (25ml) was heated on a steam bath for 1.5 hr. It was then cooled and the precipitated 3-isobutylidene-2,4-dioxo-2,3,4,5-tetrahydrofuro(3,2-c)quinoline (2) was filtered, washed successively with chloroform, aqueous sodium bicarbonate solution and water and dried. The filtrate and the chloroform washings were diluted with more chloroform and then washed with aqueous sodium bicarbonate solution and water. Evaporation of the dried extract furnished 4-hydroxy-3-isobutylidene-2-oxo-2,3-dihydrofuro(2,3-b)quinoline (3).

The physical and spectral data of 2 and 3 are given in Table - I.

Reaction of 3 with diazomethane : To a suspension of 3 (0.2g) over ether, kept at 0°C was added an ethereal solution of diazomethane (prepared from 1g of nitrosomethylurea) and the reaction mixture was stirred for 30 min. The excess reagent was decomposed and the solvent on evaporation gave 4-methoxy-3-isobutylidene-2-oxo-2,3-dihydrofuro(2,3-b)quinoline(4).

In Table - I are shown the physical and spectral data of 4.

Under similar conditions 2 was reacted with diazomethane but it was recovered quantitatively.

Synthesis of 4-hydroxy-3(1-carboxy-3-methylbut-1-enyl)-2-quinolones (5) : 2 or 3 (0.01m) was heated with aqueous NaOH (2N, 75ml) on a steam bath for 1 hr and then cooled and filtered. The filtrate on acidification furnished 5 as colourless amorphous powder.

The physical and spectral data of 5 are indicated in Table - II.

Decarboxylation of 5 : To diphenylether (30ml) kept boiling was added an intimate mixture of 5 (0.01m) and copper powder (2g) in portions over a period of 30 min. The solution was heated at reflux for a further period of 3 hr, cooled and filtered. It was placed over a column of silica gel and eluted with petroleum ether (60–80°) whereby diphenylether was removed completely. Thereafter the column was eluted with benzene - ethylacetate (4:1) when 7 was obtained as yellow crystals after evaporation of the solvent. Further elution with benzene - ethylacetate (1:1) afforded 6.

The physical and spectral data of 6 and 7 are shown in Table - II

Reaction of 6 with DDQ : A mixture of 6 (0.001m) and DDQ (0.001m) in benzene (50ml) was refluxed for 4 hr. It was then filtered and evaporated to dryness. The residue obtained was taken in chloroform and washed successively with aqueous sodium carbonate (10%) and water. Evaporation of the dried extract furnished 2,2-dimethyl-5,6-dihydropyrano(3,2-c)quinolin-5-one (8).

The vinylquinolone 7 (0.001m) on heating with DDQ (0.0015m) in benzene (50ml) for 12 hr furnished 8, identical in all respects with the one derived from 6.

The physical and spectral data of 8 are given in Table - III

Methylation of 8 : A mixture of 8 (0.2g), methyl iodide (15ml) and anhydrous potassium carbonate (10g) in dry acetone (100ml) was refluxed for 6 hr. It was filtered and the filtrate on evaporation furnished, after chromatography (SiO_2 gel, benzene) 9 as colourless needles.

The physical and spectral data of 9 are indicated in Table - III

Treatment of 6 with diazomethane : To a suspension of 6 (0.2g) over dry methanol (25ml), kept at 0°C, was added an ethereal solution of diazomethane (prepared from 1g of nitrosomethylurea) and the solution was stirred for 1 hr. The unused diazomethane was decomposed and the solution was evaporated to furnish a residue which on chromatography (SiO_2gel, benzene) gave 13.

In Table - IV are shown the physical and spectral data of 13.

Table I : Compounds 2-4 synthesised

Compound	mp°C (solvent)	Yield (%)	IR(KBr) $\nu_{max.}$ cm^{-1}	mass (m+)
2a	314-315 (acetone)	70	3090,1790,1620 1385 and 1360	255
3a	276-277 ($CHCl_3$-EtOAc)	22	3100,1795,1655, 1395 and 1355	255
2c	>320 (acetone)	65	3040,1795,1620, 1380 and 1350	285
3c	299-301 ($CHCl_3$-EtOAc)	20	3120,1790,1660, 1380 and 1355	285
2d	>320 (acetone)	63	3000,1790,1620, 1390 and 1355	..
3d	>320 ($CHCl_3$-CH_2Cl_2)	20	3010,1795,1655 1385 and 1350	315
2e	>300 (EtOAc)	68	3000,1790,1620, 1380 and 1350	315
3e	326 dec ($CHCl_3$-EtOAc)	19	3030,1795,1660 1390 and 1350	315
4c	115-116 (C_6H_6)	82	2990,1785,1640, 1395 and 1365	299

^{1}H-NMR (CCl_4): δ: 0.95(d,6H,-CH(CH_3)$_2$), 1.9(m,1H,-C$\underline{H}$(CH_3)$_2$), 3.9(s,3H,OCH_3), 4.1 (s,3H,OCH_3), 6.95(d,1H,=C$\underline{H}$—), 7.0-7.4 (m,3H,ArH)

4d	191-193 (CH_2Cl_2)	80	3000,1796,1635, 1385 and 1360	329

^{1}H-NMR ($CDCl_3$): δ: 1.15(d,6H,-CH(CH_3)$_2$), 2.15(m, 1H,-C$\underline{H}$(CH_3)$_2$), 3.9 (s,6H,2xOCH_3), 4.1 (s,3H, OCH_3), 6.15(d,1H,=C$\underline{H}$—), 6.7 and 7.3 (2s,1H each, ArH).

4e	134-135 (C_6H_6)	85	2985,1785,1630, 1385 and 1360	329

^{1}H-NMR ($CDCl_3$) : δ: 0.95(d,6H,-CH(CH_3)$_2$), 1.65(m,1H, -C$\underline{H}$(CH_3)$_2$), 3.75,3.85,3.90(3s,3H each, 3xOCH_3), 6.8(d, 1H,=C$\underline{H}$—), 7.1 and 7.6(2d,1H each, ArH).

Table II: Compounds 5-7 synthesised

Compound	mp°C (solvent)	Yield (%) From		IR(KBr) ν_{max} cm^{-1}	mass (m+)
5a	314 (EtOH)	2a 3a	100 100	3100, 2900 1780,1655	273
6a	183-184 (EtOH) lit[7] 180-182		24	3080,2995 1655	229
7a	274 dec (EtOH)		36	3080,2990 1640	229
5c	316 dec	2c 3c	90 100	3080,2995 1710,1655	..
6c	226-228 (EtOH) lit[25] 228-230; lit[8] 224-228		28	2995,1655	259
7c	301-302 (EtOH-C_6H_6)		30	3000,1650	259
5d	>320 (CH_2Cl_2-EtOH)	2d 3d	80 90	3100,2960 1740,1650	..
6d	203-204 (C_6H_6-CH_2Cl_2) lit[6] 200-201		25	2945,1645	289
7d	>320 (CH_2Cl_2-EtOH)		32	2990,1650	289
5e	>320 (C_6H_6-EtOH)	2e 3e	80 93	3110,3010 1740,1650	..
6e	217-219 (EtOH) lit[22a] 214-216		25	2995,1635	289
7e	312-314 (EtOH)		30	2990,1650	289

Table III : Compounds 8 and 9 synthesised

Compound	mp °C (solvent)	Yield (%) 6→8	Yield (%) 7→8	IR (KBr) ν_{max} cm^{-1}	^{1}H - NMR ($CDCl_3$) δ ppm: $>C<^{CH_3}_{CH_3}$ s,6H	$>C=CH-$ d,1H	Ar-CH= d,1H	ArH m	Other H	Mass M^+
8a	196-197° (MeOH) lit[1] 186-187; lit[11] 198 lit[11c] 196-198 lit[11d] 196-199	70	50	3090,1655, 1620	1.45	5.25	6.70	6.9-7.5	11.5(1H,s,NH)	227
8c	178 (C_6H_6) lit[14a] 178	75	45	2995,1660 1600	1.40	5.50	6.70	6.8-7.5	(3.9,3H,OCH_3) 9.3(1H,NH)	257
8d	209-211 (C_6H_6 - EtOH) lit[6] 210-212	78	43	2995,1655, 1600	..	..	..	..	..	..
8e	182-184 (C_6H_6 - $CHCl_3$)	70	45	3000,1660 1610	..	..	..	..	..	..
9a	85-86 (pet ether) lit[11a] 84; lit[12d] 185; lit[12b] 83-85	75 75	75	@ 2975,1670, 1613	1.45	5.25	6.65	6.9-7.5	3.7(s,3H,NCH_3)	241
9c	77-78 (C_6H_6)	80		3000,1635 1025	1.50	5.50	6.15	6.9-7.6	3.7(s,3H,NCH_3) 3.95(s,3H,OCH_3)	271
9d	150-152 (C_6H_6) lit[6] 150-155	75		2995,1630	1.60	5.20	6.50	6.9(s,1H) 7.6(s,1H)	3.6(s,3H,NCH_3) 4.05(s,6H,2xOCH_3)	301
9e	88-89 (acetone) lit[16] 87-89 lit[17] 89-90	84		*2990,1645, 1625	1.60	5.60	6.60	6.9(d,1H) 7.6(d,1H)	3.7(s,3H,NCH_3) 3.85,3.9(2s,2xOCH_3)	301

Phase * : $CHCl_3$
@ : CCl_4

Table IV : Compounds 13 and 14 synthesised

Compound	mp °C (solvent)	Yield (%)	IR ν_{max} cm^{-1}	^{1}H - NMR ($CDCl_3$) δ ppm					Mass M^+
				=C(CH_3)$_2$ 2s, 3H each	-CH=C< , t, 1H, J = 6Hz	Ar-CH- d,2H, J = 6Hz	Aromatic H m	Other H	
13a	132-134 (C_6H_6- Pet ether) lit[9] 132-134	74	* 2990,1650	1.75,1.85	5.32	3.40	6.9-7.60 7.70(dd,1H,C_5H)	3.90(s,3H,OCH_3) 13.00(br.s,1H,NH)	243
13c	119-121 (C_6H_6) lit[25] 119-120	70	@ 2995,1650	1.65,1.80	5.20	3.50	7.00-7.25 7.45(dd,1H,C_5H)	3.85,3.95 (2s,3H each, 2xOCH_3) 12.70(br.s,1H,NH)	..
13d	185-186 (CH_2Cl_2 -$CHCl_3$)	50	@ 3000,1650	insufficiently soluble					303
13e	151-153 (C_6H_6) lit[8] 151-152	40	@ 3040,1645	1.65,1.80	5.30	3.35	6.70(d,1H,C_6H) 7.50(d,1H,C_5H)	3.85,3.90,3.95, (3s,3H each, 3xOCH_3), 12.85 (br.s,1H,NH)	303
14a	Oil	70	* 2950,1630	1.65,1.90	5.55	3.35	7.0-7.60, 7.75(dd,1H,C_5H)	3.65(s,3H,NCH_3) 3.90(s,3H,OCH_3)	257
14c	Oil	70	* 2945,1635	1.60,1.75	5.30	3.25	7.00-7.60	3.70(s,1H,NCH_3), 3.80,4.00 (2s,3H each 2xOCH_3)	..
14e	86-89 (C_6H_6) lit[18] 88-89	75	*2990,1640	1.60,1.75	5.30	3.50	6.80(d,1H,C_6H) 7.50(d,1H,C_5H)	3.75(s,3H,NCH_3) 3.90(s,3H,OCH_3) 4.05(s,6H,2xOCH_3)	317

Phase * : CCl_4

@ : KBr

Treatment of 6 with methyl sulphate : To a well stirred solution of 6 (150mg) in DMF (8ml) was added powdered KOH (0.5g), followed by the addition of methyl sulphate (1.5ml). The solution was heated for 6 hr at 50-55°. It was then poured into ice water and extracted with chloroform. The chloroform extract was washed successively with aqueous sodium hydroxide solution and water. Evaporation of the dried extract furnished 14.

The physical and spectral data of 14 are given in Table - IV

ACKNOWLEDGEMENTS

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REFERENCES

1. F. Piozzi, P. Venturella and A. Bellino, Gazz. Chim. Ital., 1969,99,711.
2. M.F. Grundon, 'The Alkaloids', R.H.F. Manske and R.G.A. Rodrigo, Ed. Vol.XVII, Academic press, New York, 1977, pp 142-144.
3. P. Venturella, A. Bellino and F. Piozzi, Heterocycles, 1975, 3, 367.
4. M.F. Grundon, D.M. Harrison, M.G. Magee, M.J. Rutherford and S.A. Surgenor, Proc.R. Ir. Acad., 1983,83B,103.
5. G.M. Coppola, J. Heterocycl. Chem., 1983,20,1217.
6. M.O. Abe and D.A.H. Taylor, Phytochemistry, 1971,10,1167
7. R.M. Bowman and M.F. Grundon, J. Chem. Soc. (C), 1966,1084.
8. R. Oels, R. Storer and D.W. Young, J. Chem. Soc., Perkin Trans I, 1977,2546.
9. M. Ramesh, V. Arisvaran, S.P. Rajendran and P. Shanmugam, Tetrahedron Lett., 1982,23,967.
10. T.A. Geissman and A.K. Cho, J. Org. Chem., 1959,24,41.
11a. R.F.C. Brown, J.J. Hobbs, G.H. Hughes and E. Ritchie, Aust.J.Chem.,1954,7,348.
b. R.F.C. Brown, G.K. Hughes and E. Ritchie, Chem and Ind., 1955,1385.
c. D. Lavie, N. Danielli, R. Weitman and E. Glotter, Tetrahedron,1968,24,3011.
d. D.L.Dreyer and A. Lee, Phytochemistry, 1972, 11, 763.
e. R.M. Bowman, M.F. Grundon and K.J. James, J.Chem.Soc., Perkin Trans I,1973,1055.
f. V.I. Akhmedzhanova, I.A.Bessonova and S.Yu. Yunusov, Khim.Prir.Soedin,1974,262.
g. V.I. Akhmedzhanova, I.A. Bessonova and S.Yu. Yunusov, Khim.Prir.Soedin,1977,289.
h. I.H. Bowen and J.R. Lewis, J. Nat. Prod., 1978, 41, 184.
i. M.A. Munoz, M.R. Torres and B.K. Casels, J. Nat. Prod., 1982, 45, 367.
j. P. Tantivakana, N. Ruangrungsi, V. Vaisiriraj, D.C. Lankin, N.S. Bhacca, R.P. Borris, G.A. Cordell and L.F. Johnson, J. Org. Chem., 1983,48,268.
12a. C.D. Adams, D.R. Taylor and J.M. Warner, Phytochemistry, 1973,12,1359.
b. J. Reisch, J. Korosi, K. Szendrei, I. Novak and E. Minker, Phytochemistry, 1975,14,1678.
c. L. Jurd and A.Y. Wong, Aust. J. Chem., 1981,34,1625.
d. M.S. Hifnawy, J. Vaquette, T. Sevenent, J.L. Pusset and A. Cave, Planta Medica, 1976,29,346.
13. M. Ramesh and P. Shanmugam, Indian J. Chem. 1984, 23B,110.
14a. J.W. Huffman and T.M. Hsu, Tetrahedron Lett., 1972,141.
b. M.S. Hifnawy, J. Vaquette, T. Sevenent, J.L. Pusset and A. Cave, Phytochemistry, 1977,16,1035.
c. A.I. Gray and J.J. DeSullivan, Planta Medica, 1978, 39,203.
15. L. Ren and F. Xie, Yaouxe Xuebo, 1981,16,672; Chem. Abstr. 1982,96,48974e.
16. S.A. Khalid and P.G. Waterman, Phytochemistry, 1981,20,2761.
17. J.L. Ayafor, B.L. Sondengam and B.T. Ngadjui, Phytochemistry,1982,21,2733.
18. J.L. Ayafor and B.L. Sondengam, Tetrahedron Lett., 1980,3293.
19a. G. Cardillo, A. Cricchio and L. Merlini, Tetrahedron, 1971,27,1875.
b. J.A. Campbell, C.H. Colzadiella and N.J. McCorkindale, Tetrahedron Lett., 1966,5107.
20a. H.D. Becker, J. Org. Chem., 1969,34,1211.
b. D.L. Coffen and P.L. Garrelt, Tetrahedron Lett., 1969,2043.
21a. I.T. Eshiett and D.A.H. Taylor, J. Chem. Soc., (C), 1968,481.
b. B.D. Paul and P.K. Bose, Indian J. Chem., 1969,7,678.
22a. R. Storer and D.W. Young, Tetrahedron, 1973,29,1217.
b. V.I. Akhmedzhanova, I.A. Bessonova and S.Yu. Yunusov, Khim.Prir.Soedin., 1978,476.
23. F. Bohlmann and V.S. Bhaskar Rao, Chem. Ber., 1969,102,1774.
24a. K. Rastogi, R.S. Kapil and S.S. Popli, Phytochemistry, 1980,19,945.
b. T.S. Wu and H. Furukawa, J. Chem. Soc., Perkin Trans I, 1983,1681.
25. E.A. Clarke and M.F. Grundon, J. Chem. Soc., 1964,438.

ELEMENTAL ANALYSIS OF THE COMPOUNDS 2, 3, 4, 5, 6, 7, 8, 9, 13, and 14

Compound	Molecular Formula	Calculated C%	Calculated H%	Found C%	Found H%
2a	$C_{15}H_{13}NO_3$	70.58	5.13	70.12	4.92
2c	$C_{16}H_{15}NO_4$	67.36	5.30	67.62	5.58
2d	$C_{17}H_{17}NO_5$	64.75	5.43	64.12	5.72
2e	$C_{17}H_{17}NO_5$	64.75	5.43	64.26	5.02
3a	$C_{15}H_{13}NO_3$	70.58	5.13	69.98	5.52
3c	$C_{16}H_{15}NO_4$	67.36	5.30	67.68	5.14
3d	$C_{17}H_{17}NO_5$	64.75	5.43	65.10	5.06
3e	$C_{17}H_{17}NO_5$	64.75	5.43	65.08	5.84
4a	$C_{16}H_{15}NO_3$	71.36	5.61	71.62	5.48
4c	$C_{17}H_{17}NO_4$	68.22	5.72	68.36	5.58
4d	$C_{18}H_{19}NO_5$	65.64	5.81	65.22	5.92
4e	$C_{18}H_{19}NO_5$	65.64	5.81	65.72	5.64
5a	$C_{15}H_{15}NO_4$	65.93	5.53	66.28	5.82
5c	$C_{16}H_{17}NO_5$	63.36	5.65	63.78	5.92
5e	$C_{17}H_{19}NO_6$	61.25	5.75	61.95	5.28
6a	$C_{14}H_{15}NO_2$	73.30	6.60	73.16	6.72
6c	$C_{15}H_{17}NO_3$	69.48	6.61	69.71	6.42
6d	$C_{16}H_{19}NO_4$	66.42	6.62	66.52	6.84
6e	$C_{16}H_{19}NO_4$	66.42	6.62	66.62	6.38
7a	$C_{14}H_{15}NO_2$	73.34	6.60	73.82	6.86
7c	$C_{15}H_{17}NO_3$	69.48	6.61	69.72	6.52
7d	$C_{16}H_{19}NO_4$	66.42	6.62	66.52	6.84
7e	$C_{16}H_{19}NO_4$	66.42	6.62	66.92	6.38
8a	$C_{14}H_{13}NO_2$	73.99	5.77	74.12	5.86
8c	$C_{15}H_{15}NO_3$	70.02	5.88	70.30	6.02
8e	$C_{16}H_{17}NO_4$	66.89	5.96	66.54	5.72
9a	$C_{15}H_{15}NO_2$	74.67	6.27	74.42	6.50
9c	$C_{16}H_{17}NO_3$	70.83	6.32	71.02	6.42
9d	$C_{17}H_{19}NO_4$	67.76	6.36	67.52	6.18
9e	$C_{17}H_{19}NO_4$	67.76	6.36	67.62	6.48
13a	$C_{15}H_{17}NO_2$	74.05	7.04	74.42	7.12
13d	$C_{17}H_{21}NO_4$	67.31	6.98	67.64	7.22
13e	$C_{17}H_{21}NO_4$	67.31	6.98	67.28	6.86
14a	$C_{16}H_{19}NO_2$	74.68	7.44	74.72	7.36
14c	$C_{17}H_{21}NO_3$	71.06	7.37	71.22	7.44
14e	$C_{18}H_{23}NO_4$	68.12	7.30	68.26	7.42

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