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REVIEW

CYCLOARTANE TRITERPENOIDS

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Key Word Index—Cycloartane triterpenoids; natural occurrence; review.

Abstract—The natural occurrence of cycloartane triterpenoids is reviewed by tabulation according to structural type. Leading factors relevant to their isolation, structure determination and biosynthesis are outlined.

There is abundant evidence that cyclization of (3*S*)-squalene 2,3-epoxide [1] in algae and higher plants occurs with formation of cycloartenol (9,19-*cyclo*-5α,9β-lanost-24-en-3β-ol), and that this compound then occupies a role in sterol biosynthesis analogous to that of lanosterol in animals and fungi [2]. In keeping with these biosynthetic findings, cycloartane triterpenoids are found to be widely distributed throughout the plant kingdom [3]. The Table summarizes their occurrence* with the exception of the *Buxus* alkaloids [4]. The compounds are classified according to the nucleus (**1**–**3**; 4,4-dimethyl, 4-monomethyl and 4-desmethyl respectively) and the side chain [**A**–**E**: 23(24)-ene, 24(25)-ene, 24(28)-ene, 25(26)-ene and saturated respectively]. The majority of these compounds have been isolated by direct extraction procedures and therefore apparently occur in the free state. Their isolation as esters or methyl ethers, particularly at the 3-position, has been reported [5]. Such cases are only specifically mentioned in Table 1 when the corresponding hydroxy compound has not been adequately characterized. As with other groups of related compounds (e.g. steroids, β-amyrin triterpenoids [6]) only the more highly oxygenated members of the cycloartane group (e.g. acetyl acteol) have been isolated as glycosides.

Physical methods have beeen widely used in the identification of cylcoartane triterpenoids. The cyclopropane ring confers on these compounds characteristic NMR [7] and mass [8] spectra. It should be noted, however, that a few compounds are known in which this functional group occurs at other positions of the tetracyclic triterpene skeleton [9]. Valuable information regarding the

* Covering *Chem. Abs.* to the end of Vol. **80** (1974).

Table 1. Naturally occurring cycloartane triterpenoids

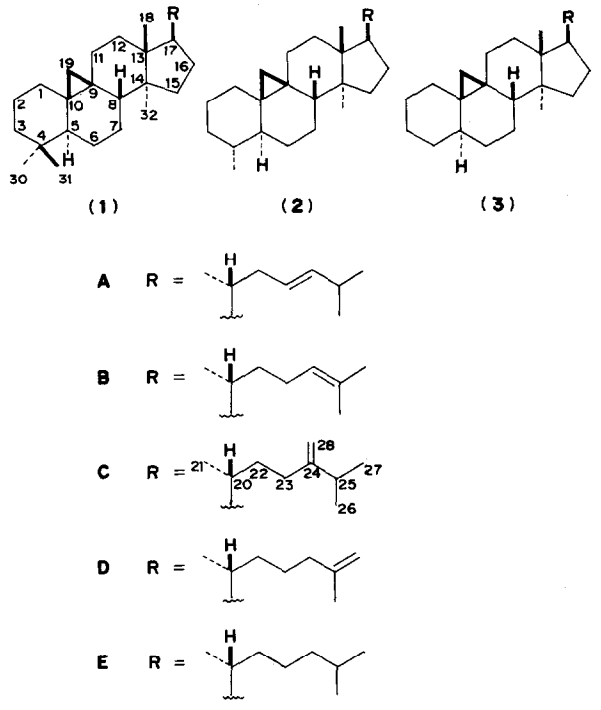
Trivial name	Structural type	Substituents	Mp (°)	$[\alpha]_D$(°)*	Occurrence	Reference
Cycloart-23-ene-3β,25-diol	**1A**†	3β,25-dihydroxy‡	200–204	38	*Tillandsia usneoides*	13
					Pachysandra terminalis	14
					Various *Euphorbia* species	15
Cyclosadol	**1A**†	3β-hydroxy-24-methyl	132–134	41	*Zea mays*	16
Cycloartenol	**1B**	3β-hydroxy	115§	54	Widespread	17
Cycloartenone	**1B**	3-keto	108–109	24	Various	18
Mangiferolic acid	**1B**	(*E*)-3β-hydroxy-26-oic acid	181–183	49	*Mangifera indica*	19
Isomangiferolic acid	**1B**	(*E*)-3α-hydroxy-26-oic acid	168–170	29	*M. indica*	20
Mangiferonic acid	**1B**	(*E*)-3-keto-26-oic acid	187–189	24	*M. indica*	20
					Shorea acuminata	21

Table 1.—*cont.*

Trivial name	Structural type	Substituents	Mp (°)	$[\alpha]_D$(°)*	Occurrence	Reference
Hydroxymangiferolic acid	1B	(*E*?)-3β,27-dihydroxy-26-oic acid	201–204	39	*M. indica*	20
Hydroxymangiferonic acid	1B	(*E*?)-27-hydroxy-3-keto-26-oic acid	190–192	18	*M. indica*	22
Cimicifugenol	1B	3β-hydroxy-7-ene	112–113	21	*Cimicifuga* species	11
Cyclograndisolide	1B	(23*R*)-3α-methoxy-26,23-olide	191–193	‖	*Abies grandis*	23
Epicyclograndisolide	1B	(23*S*)-3α-methoxy-26,23-olide	193–194	‖	*A. grandis*	23
Cyclobranol	1B	3β-hydroxy-24-methyl	156–157	38	Rice bran oil	24
—	1B†	3β-hydroxy-24-methyl-26-al	166–170	41	*Mangifera indica*	25
Nigranoic acid	1B	(*Z*)-3,4-seco-4(30)-ene-3,26-dioic acid	—	56 (MeOH)	*Schizandra nigra*	26
31-Norcycloartenol	2B	3β-hydroxy	93–95		*Carnegiea gigantea*	27
		(3-acetate)		63		
24-Methylenecycloartanol	1C	3β-hydroxy	121–122	43	Widespread	28
24-Methylenecycloartanone	1C	3-keto	111–112	20	Various	28
Cyclomahogenol	1C	3β,16β-dihydroxy	151–152	42	*Swietenia mahagoni*	29
24-Methylenecycloart-3,26-diol	1C	(25*R*)-3β,26-dihydroxy	154–157	54	*Mangifera indica*	25, 30
Ambolic acid	1C	(25*R*)-3β-hydroxy-26-oic acid	167–169	31	*M. indica*	30, 31
Ambonic acid	1C	(25*R*)-3-keto-26-oic acid	149–150	9	*M. indica*	30, 32
Cycloeucalenol	2C	3β-hydroxy	140	45	Widespread	33
Cycloeucalenone	2C	3-keto	81–83	53	*Musa sapientum*	34
Cyclofuntumienol	2C	(*Z*)-3β-hydroxy-28-methyl	143–145	50	*Funtumia elastica*	35
24-Methylenepollinastanol	3C	3β-hydroxy	115–117	—	*Musa sapientum*	36
					Chlorella emersonii	37
Surianol	3C	3β,4α-dihdroxy	173–174	39	*Suriana maritima*	38
Isocycloartenol	1D	3β-hydroxy	92–94	45	*Artocarpus chaplasha*	39
≡ β-Cyclo-orysterol?					Rice bran oil	40
Cycloart-25-ene-3β,24ξ-diol	1D	3β,24ξ-dihydroxy	184–188	48	*Tillandsia usneoides*	13
					Pachysandra terminalis	14
3β-Hydroxycycloart-25-en-24-one	1D	3β-hydroxy-24-keto	133–136		*Tillandsia usneoides*	13
		(3-acetate)		58		
Cyclolaudenol	1D	(24*S*)-3β-hydroxy-24-methyl	125	46	Widespread	41, 42
Cycloneolitsin	1D	3β-methoxy-24,24-dimethyl	169–174	63	*Neolitsea dealbata*	43
Cyclobalanone	1D	3-keto-24,24-dimethyl	187–190	20	*Quercus glauca*	44
Dehydroxy-15-*O*-methyl-cimigenol	1D	(23*R*, 24*S*)-16β,23;16α,24-diepoxy-3β-hydroxy-15α-methoxy	222–223	39	*Cimicifuga acerina*	45
31-Norcyclolaudenol	2D	(24*S*)-3β-hydroxy-24-methyl	139–140	44	*Polypodium vulgare*	46
					Musa sapientum	34
31-Norcyclolaudenone	2D	(24*S*)-3-keto-24-methyl	130–132	49	*M. sapientum*	47
Cyclotrichosantol	2D	3β-hydroxy-24ξ-ethyl	143–144	42	*Trichosantes palmata*	48
Cycloartanol	1E	3β-hydroxy	101–102	51	Various	49
25-Hydroxycycloartanol	1E	3β-25-dihydroxy¶	181–182	49	Rice bran ferulates	50
—	1E	3β-hydroxy-24ξ-methoxy-24-methyl	151	43	Rice bran ferulates	50
Argentatine A	1E	16β,25-dihydroxy-20ξ,24ξ-epoxy-3-keto	—	—	*Parthenium argentatum*	51
Argentatine B	1E	16β,23ξ-epoxy-25-hydroxy-3-keto-24ξ-methyl	—	—	*P. argentatum*	51
Argentatine C	1E	16β,23ξ,24ξ-trihydroxy-3-keto-24-methyl	—	—	*P. argentatum*	51
Aglycone A	1E	(23*R*,24*S*)-16α,23-epoxy-3β,24,25-trihydroxy-15-keto	220–225	46	*Cimicifuga* (*Actea*) *racemosa*	52
≡ Dahurinol?			237–238	55	*C. dahurica*	53
Cimigenol	1E	(23*R*,24*S*)-16β,23;16α,24-diepoxy-3β,15α,25-trihydroxy**	222–224	45	Various *Cimicifuga* species	45, 54
Acetyl acteol	1E	(23*R*,24*S*,25*R*)-12β-acetoxy-3β,27ξ-dihydroxy-16β,23;23,27;24,25-triepoxy	248–249	−80	*Actea racemosa*	55
27-Deoxy acetyl acteol	1E	(23*R*,24*S*,25*R*)-12β-acetoxy-3β-hydroxy-16β,23;23,27;24,25-triepoxy	289–292 (dec.)	−88	*Cimicifuga racemosa*	56
31-Norcycloartanol	2E	3β-hydroxy	128–132	49	*Polypodium vulgare*	49
					Smilax aspera	57
					Taraxacum dens-leonis	58
Pollinastanol	3E	3β-hydroxy	111–112	35	Compositae	59
					Polypodium vulgare	
					Smilax medica	

* For solutions in chloroform.
† Configuration of the double bond unknown.
‡ Also occurs as the 25-*O*-methyl derivative.
§ Mp 99° when solvated.
‖ See Ref. [23] for ORD and CD data.
¶ Also occurs as the 25-*O*-ethyl derivative.
** Also occurs as the 15-*O*-methyl, or 25-*O*-methyl, or 25-*O*-acetyl derivatives.

In our opinion the best source of cycloartenol is *Strychnos nux-vomica* [17] and its 24-methylene derivative and cycloeucalenone may be obtained from banana fruit skin [34].



degree of methylation at C-4 is available from the ORD spectra of 3-ketones [10].

Analysis of the Table indicates the following distribution of compounds: type (**1**), 38; (**2**), 8; (**3**), 3. Type **A**, 2; **B**, 14; **C**, 11; **D**, 10; and **E**, 12. The invariable presence of the 14α-methyl group is understandable in biosynthetic terms. Thus, it is known [2] that removal of this group from tetracylcic triterpenoids is associated with the presence of a double bond at position 7 or 8, and the latter is normally generated only as a consequence of cleavage of the 9β,19-cyclopropane ring (but see cimicifugenol [11]). The lack of any definitive relationship between the degree of demethylation at C-4 and the state of modification of the side chain suggests the existence of a biosynthetic grid in which a number of transformation but not substrate specific enzymes act with moderate independence of one another. This would parallel the biosynthesis of ergosterol in *Saccharomyces cerevisiae* [12].

Finally, we would note the lack of any cycloartane compounds substituted at C-21. With other tetracyclic triterpenoids [3] this is one of the most frequently functionalized sites.

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REFERENCES

1. Boar, R. B. and Damps K. (1974) *Tetrahedron Letters* 3731; Barton, D. H. R., Jarman, T. R., Watson, K. G., Widdowson, D. A., Boar, R. B. and Damps, K. (1974) *Chem. Commun.* 861.
2. Goad, L. J. and Goodwin T. W. (1972) in *Progress in Phytochemistry* (Reinhold, L. and Liwschitz, Y., eds.), Vol. 3, p. 113. Interscience, London; Goodwin, T. W. (1973) in *Recent Advances in Phytochemistry* (Runeckles, V. C. and Mabry, T. J., eds.), Vol. 6, p. 97. Academic Press, New York.
3. Boiteau, P., Pasich, B. and Rakoto Ratsimamanga, A. (1964) *Les Triterpenoides en Physiologie Vegetale et Animale*, Gauthier-Villars, Paris; Ourisson, G., Crabbe, P. and Rodig, O. R. (1964) *Tetracyclic Triterpenes*, Hermann, Paris; Connolly, J. D. and Overton, K. H. (1972) in *Chemistry of Terpenes and Terpenoids* (Newman, A. A., ed.). Academic Press, London; Scott, A. I. and Devon, T. K. (1972) *Handbook of Naturally Occurring Compounds*, Vol. 2 *Terpenes*, Academic Press, London.
4. Cerny, V. and Sorm, F. (1967) in *The Alkaloids* (Manske, R. H. F., ed.), Vol. 9, p. 375. Academic Press, New York.
5. See for example, Knapp, F. F. and Nicholas, H. J. (1969) *Phytochemistry* **8**, 207.
6. Boar, R. B. and Allen, J. (1973) *Phytochemistry* **12**, 2571.
7. Iavarone, C., Piancatelli, G., Mincione, E. and Nicita, G. (1970) *Gazz. Chim. Ital.* **100**, 888; Cheung, H. T., Wong, C.-S. and Yan, T. C. (1969) *Tetrahedron Letters* 5077; ref. 46.
8. Audier, H. E., Beugelmans, R. and Das, B. C. (1966) *Tetrahedron Letters* 4341; Aplin, R. T. and Hornby, G. M., (1966) *J. Chem. Soc.* (*B*) 1078; Wyllie, S. G. and Djerassi, C. (1968) *J. Org. Chem.* **33**, 305.
9. Hale, R. L., Leclercq, J., Tursch, B., Djerassi, C., Gross, R. A., Weinheimer, A. J., Gupta, K. and Scheuer, P. J. (1970) *J. Am. Chem. Soc.* **92**, 2179; Sheikh, Y. M., Djerassi, C. and Tursch, B. M. (1971) *Chem. Commun.* 217; Ferguson, G., Gunn, P. A., Marsh, W. C., McCrindle, R., Restivo, R., Connolly, J. D., Fulke, J. W. B. and Henderson, M. S. (1973) *Chem. Commun.* 159.
10. Djerassi, C., Halpern, O., Halpern, V. and Riniker, B. (1958) *J. Am. Chem. Soc.* **80**, 4001.
11. Takemoto, T., Kusano, G. and Yamamoto, N. (1970) *Yakugaku Zasshi* **90**, 68.
12. Barton, D. H. R., Corrie, J. E. T., Widdowson, D. A., Bard, M. and Woods, R. A. (1974) *J. Chem. Soc. Perkin I* 1326.
13. Djerassi, C. and McCrindle, R. (1962) *J. Chem. Soc.* 4034.
14. Kikuchi, T., Toyoda, T., Arimoto, M., Takayama, M. and Yamano, M. (1969) *Yakugaku Zasshi* **89**, 1358.
15. Ponsinet, G. and Ourisson, G. (1967) *Phytochemistry* **6**, 1235.
16. Pinhas, H. (1969) *Bull. Soc. Chim. Fr.* 2037.
17. Bentley, H. R., Henry, J. A., Irvine, D. S. and Spring, F. S. (1953) *J. Chem. Soc.* 3673.
18. Barton, D. H. R. (1951) *J. Chem. Soc.* 1444.
19. Corsano, S. and Mincione, E. (1965) *Tetrahedron Letters* 2377.
20. Corsano, S. and Mincione, E. (1967) *Ann. Chim.* (*Rome*) **57**, 508.
21. Cheung, H. T. and Yan, T. C. (1972) *Austral. J. Chem.* **25**, 2003.
22. Corsano, S. and Piancatelli, G. (1965) *Ric. Sci. Rend. Sez. A* **8**, 484.
23. Kutney, J. P., Grierson, D. S., Knowles, G. D., Westcott, N. D. and Rogers, I. H. (1973) *Tetrahedron* **29**, 13.

24. Tachibana, K., Endo, T. and Misumi, T. (1970) *Chem. Abstr.* **73,** 4058.
25. Corsano, S. and Mincione, E. (1967) *Ric. Sci.* **37,** 370.
26. Kikuchi, M. and Yoshikoshi, A. (1972) *Chem. Letters* 725.
27. Devys, M., Alcaide, A. Pinte, F. and Barbier, M. (1970) *Tetrahedron Letters* 4621.
28. Ohta, G. (1960) *Chem. Pharm. Bull (Tokyo)* **8,** 5 and 9.
29. Chakraborty, D. P., Basak, S. P., Das, B. C. and Beugelmans, R. (1971) *Phytochemistry* **10,** 1367.
30. Corsano, S. and Mincione, E. (1968) *Chem. Commun.* 738.
31. Corsano, S. and Mincione, E. (1966) *Ric. Sci.* **36,** 494.
32. Corsano, S. and Mincione, E. (1967) *Ann. Chim. (Rome)* **57,** 522.
33. Cox, J. S. G., King, F. E. and King, T. J. (1956) *J. Chem. Soc.* 1384; (1959) *J. Chem. Soc.* 514.
34. Boar, R. B., McGhie, J. F. and Romer, C. R., unpublished observations.
35. Mukam, L., Charles, G., Hentchoya, J., Njimi, Th. and Ourisson, G. (1973) *Tetrahedron Letters* 2779.
36. Knapp, F. F., Phillips, D. O., Goad, L. J. and Goodwin, T. W. (1972) *Phytochemistry* **11,** 3497.
37. Doyle, P. J., Patterson, G. W., Dutky, S. R. and Thompson, M. J. (1972) *Phytochemistry* **11,** 1951.
38. Mitchell, R. E. and Geissman, T. A. (1971) *Phytochemistry* **10,** 1559.
39. Mahato, S. B., Banerjee, S. K. and Chakravarti, R. N. (1971) *Phytochemistry* **10,** 1351.
40. Yoshida, S., Takasaki, R. and Sueyoshi, H. (1956) *Yakugaku Zasshi* **76** 1333.
41. Henry, J. A., Irvine, D. S. and Spring, F. S. (1955) *J. Chem. Soc.* 1607.
42. Cyclolaudenone, the corresponding 3-ketone, has been detected in opium marc but could only be isolated after reduction to cyclolaudenol—Dutta, N. L. and Quasim, C. (1969) *Indian J. Chem.* **7,** 1276.
43. Ritchie, E., Senior, R. G. and Taylor, W. C. (1969) *Austral. J. Chem.* **22,** 2371.
44. Tachi, Y., Taga, S., Kamano, Y. and Komatsu, M. (1971) *Chem. Pharm. Bull. (Tokyo)* **19,** 2193.
45. Takemoto, T. and Kusano, G. (1969) *Yakugaku Zasshi* **89,** 954.
46. Berti, G., Bottari, F., Macchia, B., Marsili, A., Ourisson, G. and Piotrowska, H. (1964) *Bull. Soc. Chim. Fr.* 2359.
47. Knapp, F. F. and Nicholas, H. J. (1970) *Steroids* **16,** 329.
48. Kocor, M. and St. Pyrek, J. (1973) *J. Org. Chem.* **38,** 3688.
49. Berti, G., Bottari, F., Marsili, A., Morelli, I. and Polvani, M. (1967) *Tetrahedron Letters* 125.
50. Endo, T., Naito, S. and Inaba, Y. (1970) *Yukagaku* **19,** 298 and 302.
51. Rodriguez-Hahn, L., Romo de Vivar, A., Ortega, A., Aguilar, M. and Romo, J. (1970) *Rev. Latinoamer. Quim.* **1,** 24.
52. Piancatelli, G. (1971) *Gazz. Chim. Ital.* **101,** 139.
53. Sakurai, N., Inoue, T. and Nagai, M. (1972) *Yakugaku Zasshi* **92,** 724.
54. Corsano, S. and Piancatelli, G. (1969) *Gazz. Chim. Ital.* **99,** 1140; Takemoto, T., Kusano, G. and Kawahara, M. (1970) *Yakugaku Zasshi* **90,** 64.
55. Corsano, S., Piancatelli, G. and Scettri, A. (1971) *Gazz. Chim. Ital.* **101,** 797.
56. Linde, H. (1968) *Arch. Pharm.* **301,** 335.
57. Ayenger, K. N. N. and Rangaswami, S. (1967) *Tetrahedron Letters* 3567.
58. Devys, M., Andre, D. and Barbier, M. (1969) *C. R. Acad. Sci., Ser. D* **269,** 798.
59. Ducruix, A., Pascard-Billy, C., Devys, M., Barbier, M. and Lederer, E. (1973) *Chem. Commun.* 929.