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APPLICATION OF THE METHOD OF MOLECULAR ROTATION DIFFERENCES IN STRUCTURAL AND STEREOCHEMICAL PROBLEMS IN TRITERPENES

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Abstract—In the literature of 105 unsaturated tetracyclic and pentacyclic triterpenoid alcohols and their simple derivatives have been correlated by the Barton and Jones Method of Molecular Rotation Differences (MRD). By so doing, all the known compounds have been divided into nineteen stereoskeletal types with diagnostic, in some cases, values of MRD. New generalisations are made on the application of this method to the elucidation of structures of triterpenoids. Cases in the literature in which the reported specific rotation values are at variance with the established structures are indicated for future investigation and correction, especially in the more serious ones.

A relationship between the changes in molar optical rotations (ΔM) of triterpenoid alcohols upon acetylation (ΔM_1), benzoylation and oxidation (ΔM_2 in this paper) and their basic stereoskeleton was first recognised by Barton and Jones.[1] They showed that ΔM values were characteristic of the basic stereoskeleton of the molecule. On the basis of their ΔM values, they were able to classify the known triterpenoids, whose structures were then incompletely established, into three groups: the α- and β-amyrin group, the lupeol-betulin group and a new group consisting of 3β-hydroxyeupha-8,24-diene, 3β-hydroxyolean-18-ene, 3β-hydroxyurs-20(30)-ene, 3β-hydroxyurs-20-ene and 3β-hydroxylanosta-8,24-diene eight others being left unclassified. Barton and Jones elegantly demonstrated the usefulness of this structural tool by immediately exploiting it in resolving a number of structural anomalies then in the literature. Barton, in a series of papers,[2,3] later extended these studies to steroidal compounds and thereby established that the position of nuclear C=C in steroids was indicated by their ΔM values, and proceeded to classify this class of compounds accordingly.

The generalisations of Barton and Jones were unavoidably based essentially on data collected on triterpenoids of the oleanane, ursane and lupane skeletons with C=C variously located at C-12, in ring E, or on ring E side chain. However, a number of later workers (see, e.g. Refs. 4–9) have successfully applied the same general principles in the elucidation of triterpenoid structures of various stereoskeletal types with the C=C in other positions, especially C-5, C-7, C-8 and C-9(11), by comparing their ΔM (usually ΔM_1 or ΔM_2 alone) values with those of a few selected known structures. No attempt has been made so far to classify the now known vast number of triterpenoids whose structures are well established into different stereoskeletal types on the basis of their ΔM values for ease of reference and application in structural studies.

It is the aim of this paper to carry out this classification, and hence to amplify the scope of the application of the MRD as a diagnostic tool for the rapid identification of known triterpenoids and classification of new ones.

Scope of coverage

In this paper, molecular rotations $[M]_D$ data have been collated for mostly naturally occurring tetracyclic and pentacyclic, generally monohydric (C-3), triterpenoid alcohols (together with their acetates and ketones) containing 4,4-dimethyl groups with no substitution in ring A (in order to minimise vicinal action[10]) whose structures have been firmly established. An examination of a number of examples (not listed here) in different stereoskeletal classes showed that when any other hydroxy group (apart from the C-3-hydroxy) in the molecule is acetylated or oxidised concurrently with the C-3-hydroxyl, the resulting ΔM values do not correlate well with one another. Since carboxylic acids are normally in equilibrium with their dimers, and since this equilibrium is sensitive to concentration and structure, only data on the esters of triterpenoid carboxylic acids have been considered. In doing so, a number of anomalies previously observed in this and in previous works were eliminated. All the compounds with 5, 7, 8, 9(11), 7, 9(11) and 14 C=C found in the literature with the necessary data have been considered. No attempt has been made to include all the known compounds with Δ^{12} or with the C=C in ring E or outside ring E, partly on the grounds of the earlier work[1] and partly on the grounds of the ready agreement of all the data considered for these two classes of compounds.

Calculation of $[M]_D$ values

The excellent book[11] by Boiteau *et al.* has been a most useful source of information on compounds known by 1962. However references have been made to the original literature cited and to more recent ones in cases of serious disparity in the values of specific rotations quoted. A major problem in this exercise is the poor agreement, in many cases, between the values of specific rotations (measured in the same solvent and similar concentrations using Na_D light) quoted in the literature for the same compound. As much as possible, the arithmetic mean of the quoted values have been used. However, in a number of cases, those values which give better agreement with those of other members of the same group in which there is no recorded discrepancy, have been selected. The common errors in the determination of specific rotations have been adequately discussed by Barton and Jones[1] and by Barton and Klyne.[3] In order to minimise errors arising from effects of solvent and temperature,[3] only values recorded in chloroform at normal room temperature have been used. In spite of this, judging from the range of values com-

monly found in the literature, a margin of error of ± 10% in ΔM must be considered good.

RESULTS AND DISCUSSION

When all the ΔM values were examined alongside the full structures of the triterpenoids, a classification according to the position of C=C was immediately apparent. Further scrutiny revealed the possibility of further classification according to their basic stereoskeletons up to C/D ring junction (with the same position of C=C) and finally according to the configuration at C-3 (with the same stereoskeleton and the same position of C=C). Consequently, taking these three factors into consideration, it was possible to divide all the known unsaturated tetracyclic and pentacyclic triterpenes into nineteen structural types on the basis of their ΔM_1 and ΔM_2 values considered together. The possibility of the existence of additional three types containing known stereoskeleton, but with C-3α-OH is obvious. However, for clarity of presentation and discussion, all the compounds have been divided into eight main groups according to the position of the C=C; each group was then subdivided into classes according to their basic stereoskeleton and the configuration at C-3.

A summary of the average ΔM values for each structural type is presented in Table 1. In arriving at the average ΔM values in Table 1, figures which are greatly at variance with the majority of the others in the same class are not taken into consideration. Such figures are considered erroneous, and reasons are advanced, where possible, in support. In cases where the available data are either insufficient, or are greatly at variance with one another, no averages are recorded. A provisional average indicates one which is subject to revision when more data are available, a reasonable one indicates one which could still be improved upon.

An analysis of Table 1 reveals some definite trends upon which the following generalisations are based:

(i) When accurately measured (on pure specimens) specific rotation data are available, it is possible to quickly assign a triterpenoid to one of eleven of the listed structural types for which complete data are available, and hence fix its stereoskeleton, including its configuration at C-3, up to ring C/D junction. This possibility will no doubt facilitate the direction of further structural work on the compound. In the only one case (Δ^5 compounds class A, and Δ^7 compounds) in which the ΔM values are similar, a differentiation can be readily made by the aid of mass spectroscopy.[4,6,12,13]

(ii) The assignment of basic stereoskeleton and the position of C=C in these compounds on the basis of their ΔM values is most reliable when *both* values of ΔM_1 and ΔM_2 are available. A successful use of either of them alone, as common in the literature, must now be regarded as fortituous with the sole exception of Δ^{12} and $\Delta^{13(18)}$ compounds, which, unlike all other structural types, generally give negligible ΔM_1 values. In this respect, when both ΔM_1 and ΔM_2 values are considered, 3β-hydroxyolean-18-ene, 3β-hydroxyurs-20(30)-ene and 3β-hydroxyurs-20-ene must belong to the same group as 3β-hydroxylup-20(29)-ene and methyl 3β-hydroxylup-20(29)-en-28-oate; and 3β-hydroxyeupha-8,24-diene to a different group (3A) contrary to earlier[1] classification when necessary data were not yet available.

(iii) Only compounds with the same configuration at C-3 can be correlated with one another. This observation now explains the observed discrepancy between the ΔM_1 values of methyl 3α-hydroxyolean-12-en-24-oate and methyl 3α-hydroxyurs-12-en-24-oate (which have C-3α-OH and are in Group 6B in this paper) and those of the other members of the then α- and β-amyrin group (which have C-3β-OH and are in Group 6A in this paper). This view is further substantiated by the fact that the ΔM values for methyl 3α-hydroxyolean-12-en-29-oate and methyl 3α-hydroxyolean-12-en-28-oate are in good agreement with those of the former two compounds. Thus ΔM values may be used to fix not only the basic stereoskeleton and the position of C=C in a new compound, but also the configuration at C-3.

(iv) The configuration of C-3-hydroxyl is at present determined by the fact that C-3-axial and equatorial protons in triterpenoid alcohols and their acetates absorb at different characteristic frequencies in the NMR.[14] However the presence of other protons in similar stereoelectronic environment in the molecule could make ready

Table 1. Average ΔM values of triterpenoid structural types

Group	Position of C=C	Config. at C-3	ΔM_1	ΔM_2	Comments
1 A	5	β	+ 112.5	- 131.5	Reliable
B	5	α	- 42.5	- 119.5	Reliable
2	7	β	+ 107	- 125	Reliable
3 A	8	β	+ 42	+ 198	Reasonable
B	8	α	—	+ 228	ΔM_1 not possible, ΔM_2 good
C	8	β	+ 28.5	+ 97	ΔM_1 almost negligible, ΔM_2 reasonable
D	8	α	- 218	—	ΔM_1 reliable, ΔM_2 not possible
4 A	9(11)	β	—	—	Averages not possible
B	9(11)	α	—	—	Only one member known
C	9(11)	β	+ 92	- 75	ΔM_1 reliable, ΔM_2 provisional
D	9(11)	α	—	—	Averages not possible
5 A	7,9(11)	β	+ 131	- 76	ΔM_1 reliable, ΔM_2 provisional
B	7,9(11)	β	—	—	Averages not possible
6 A	12,13(18)	β	≈ 0	—	ΔM_1 reliable, ΔM_2 aver. not possible
B	12,13(18)	α	- 146.5	—	ΔM_1 reliable, no ΔM_2 data
7 A	14	β	+ 39	+ 55	ΔM_1 reasonable, ΔM_2 provisional
B	14	α	—	—	Only one member known
8A	in ring E or outside	β	+ 60.5	+ 146	most reliable averages
B		α	- 80.5	+ 218	Reasonable

assignment of chemical shifts and the determination of appropriate coupling constants difficult. However in the present work it is observed that, whereas ΔM_1 values for C-3β-hydroxyl compounds (including virtually all other known ones not listed in this paper) are either positive or negligible, ΔM_1 values for C-3α-hydroxyl compounds are always negative. The only exceptions to this generalisation 3β-hydroxyeupha-8,24-diene[11,15] (Group 3A) 3β-hydroxyfern-8-ene[6] (Group 3A), 3β-hydroxy-16-23-epoxylanosta-8,22,24-triene[16] (Group 3C), 3β-hydroxybaura-7,9(11)-diene[11] (Group 5B), 3β-hydroxyhop-28-ene[17] (Group 8A) and 3α-hydroxyolean-18-ene[11] (Group 8B) are cases in which their ΔM values are already greatly at variance with their respective group averages (see below) and are therefore considered erroneous.

The ΔM_1 values therefore provide an additional tool for a quick determination of the configuration at C-3. Furthermore, in all the cases found in the literature, the C-3β-compounds have much higher ΔM_1 values, but lower or similar ΔM_2 values than the 3α-epimers. This observation provides a useful check on the accuracy of specific rotation data on C-3-epimeric alcohols.

(v) Of all the compounds found, only those compounds with Δ^5, Δ^7, $\Delta^{9(11)}$ and $\Delta^{7,9(11)}$ unsaturation, irrespective of their basic stereoskeleton and configuration at C-3, have negative ΔM_2 values. There are good reasons to doubt the reliability of the specific rotation data recorded on the only one exceptional case. A figure of +140 is calculated for 3α-hydroxylanosta-9(11)-en-26,23-olide[18] compared with −20 for 3α-hydroxyarbor-9(11)-ene[19] in the same group 4C.

(vi) Δ^8 and $\Delta^{9(11)}$ Pentacyclic triterpenoids give virtually identical mass spectra[6] and can therefore not be differentiated by this technique. In such a situation one would normally have to resort to infrared and NMR evidences, where possible to settle the differentiation. However this differentiation is readily achieved[20] by the MRD method (see Table 1).

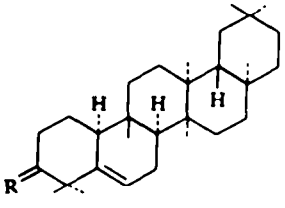
Having discussed the general trends noticeable in all the groups, it is pertinent to highlight the peculiarities of each group and class with a view to focussing attention on those members whose specific rotation values do not tally with their structures. Though it is likely that these erroneous data are due to impurity of sample and experimental errors in the actual measurement of the optical rotation, the possibility of wrong structures cannot be completely ruled out in a few cases. Attempts will be made in a continuation of this work to correct these anomalies wherever possible.

1. *Group* 1 (Δ^5 compounds). There is good agreement between the ΔM values for all the few known members of both Classes A and B. A. G. Gonzalez and co-workers recently isolated the triterpenoid alcohol guimarenol from the plant *Ceropegia dichotoma*, and on the basis of several physico-chemical evidences assigned[21] to it the partial structure (5). However considering its ΔM_1 and ΔM_2 values of +107 and −127 respectively, the proposed partial structure can now be improved to (6) leaving only the stereochemistry of the D/E ring junction and the relative configuration of the *iso*-propyl group to be settled.

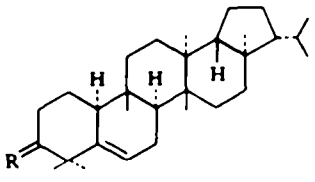
2. *Group* 2 (Δ^7 compounds). Members of this group have the euphane skeleton with C-3β-hydroxyl group, with the exception of 3β-hydroxylanost-7-ene[7,11] which has a lanostane skeleton. These two stereoskeletons are clearly differentiated from each other in the Δ^8 compounds by their ΔM (especially ΔM_2) values (see Group 3 below), but the distinction is less clear with $\Delta^{7,9(11)}$ compounds (though the data in the latter group are still rather scanty, see Group 5). It is therefore surprising that both ΔM_1 and ΔM_2 values, which appear quite reliable, for methyl 3α-hydroxyolean-12-en-28-oate are in good agreement with those of the former two compounds. Thus ΔM values may be used to fix not only the basic stereoskeleton and the position of C=C in a new compound, but also the configuration at C-3.

3. *Group* 3 (Δ^8 compounds). Four structural types are distinguishable in this group, depending on whether the compound has a lanostane or euphane skeleton and whether the C-3-hydroxyl is α or β. Members of Class A possess the euphane skeleton with C-3β-hydroxyl. In this class it is quite clear that both ΔM values for 3β-hydroxyeupha-8,24-diene[11,15] and ΔM_1 for 3β-hydroxyfern-8-ene[6] are quite erroneous, whereas those

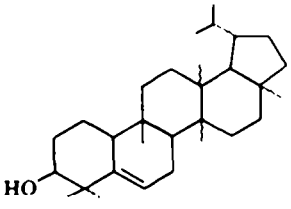
GROUP 1



1: R = H (β-OH)
3: R = H (α-OH)



2: R = H (β-OH)
4: R = H (α-OH)



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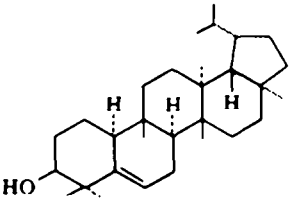
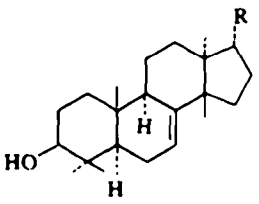
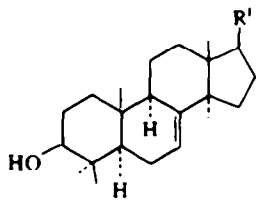


6

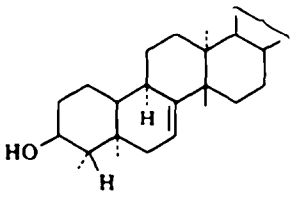
GROUP 2

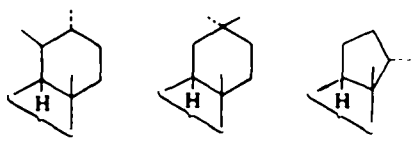


7: R = $CH(CH_3)(CH_2)_2CH{=}C(CH_3)COOCH_3$
8: R = $CH(CH_3)(CH_2)_3CH(CH_3)COOCH_3$
9: R = $CH(CH_3)(CH_2)_2CH{=}C(CH_3)_2$
10: R = $CH(CH_3)(CH_2)_3CH(CH_3)_2$



11: R' = $CH(CH_3)(CH_2)_3CH(CH_3)_2$

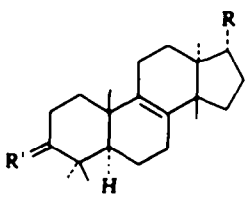




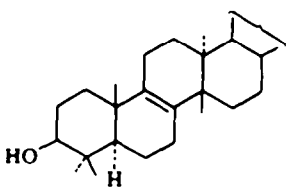
12 13 14

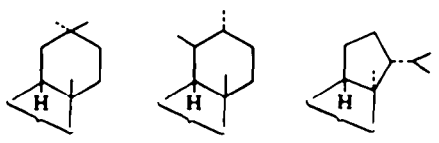
GROUP 3

Class A



15: R = $CH(CH_3)(CH_2)_2CH{=}C(CH_3)_2$, R' = H ($\beta$-OH)
16: R = $CH(CH_3)(CH_2)_3CH(CH_3)_2$, R' = H ($\beta$-OH)
17: R = $CH(CH_3)(CH_2)_2CH{=}C(CH_3)COOCH_3$, R' = H ($\beta$-OH)
21: R = $CH(CH_3)(CH_2)_2C(=CH_2)CH(CH_3)_2$, R' = H ($\beta$-OH)
22: R = $CH(CH_3)(CH_2)_2CH{=}C(CH_3)CH_2OH$, R' = H ($\beta$-OH)
23: R = $CH(CH_3)(CH_2)_2CH{=}C(CH_3)_2$, R' = H ($\beta$-OH) (C-20 epimer of 15)



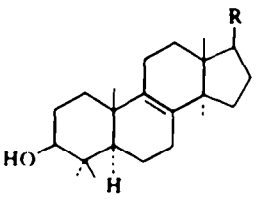


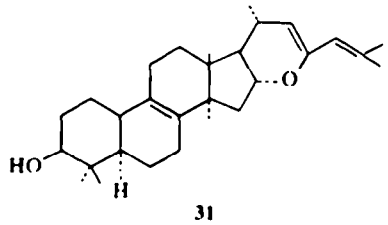
18 19 20

Class B

24: R = $CH(COOCH_3)(CH_2)_2CH{=}C(CH_3)_2$, R' = H ($\alpha$-OH)
26: R = $CH(CH_3)(CH_2)_3CH(CH_3)COOCH_3$, R' = H ($\alpha$-OH)
27: R = $CH(CH_3)(CH_2)_2CH{=}C(CH_3)COOCH_3$, R' = H ($\alpha$-OH)

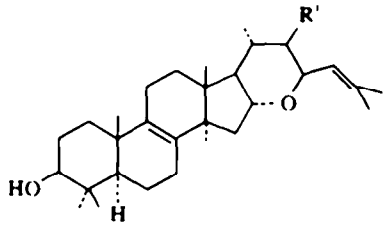
Class C





31

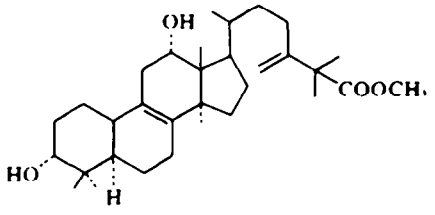
28: R = $CH(CH_3)(CH_2)_2CH{=}C(CH_3)_2$
29: R = $CH(COOCH_3)(CH_2)_2CH{=}C(CH_3)_2$
30: R = $CH(CH_3)(CH_2)_2CH(CH_3)_2$
34: R = $CH(CH_3)(CH_2)_2C(=CH_2)CH(CH_3)_2$
35: R = $CH(COOCH_3)(CH_2)_2C(=CH_2)CH(CH_3)_2$
36: R = $CH(CH_3)(CH_2)_2CH(CH_3)_2$, 14α-H



32: R' = OAc
33: R' = OH

Class D

37: C-3-epimer of 30
38: C-3-epimer of 29
39: C-3-epimer of 31
40: C-3-epimer of 33
41a: C-3-epimer of 32



41b

for 3β-,26-dihydroxyeupha-8,24-diene and ΔM_2 for 3β-hydroxyfern-8-ene need some correction. 3β-Hydroxyeupha-8,24-diene and its derivatives appear quite difficult to obtain pure, judging from their physical constants in the literature:[18,32] alcohol: $[\alpha]_D$ −2.5 ± 6.5°, +5°; acetate: $[\alpha]_D$ − 10.5 ± 6.5°; ketone − 72°, +16°. Fern-8-en-3β-ol was obtained from the hydrolysis of the acetate which in turn was obtained[6] as follows. The mixture of products formed on acid-induced migration reaction of 3β-methoxyfern-9-ene was resolved by column chromatography to give the unreacted ether $[\alpha]_D$ − 5.3° as the first eluate followed by Δ⁸-fernenyl acetate $[\alpha]_D$ + 20.3° and finally a mixture of the acetate and another compound $[\alpha]_D$ − 74.7° (later obtained from the mixture by fresh chromatography). It is therefore conceivable that the sample of Δ⁸-fernenyl acetate on which the recorded $[\alpha]_D$ was measured might have been significantly contaminated by this other compound. In Class C, it is clear that the optical rotation data on 3β-hydroxy-16,23-epoxylanosta-8,22,24-triene,[16] 3β-22-di-hydroxy-16,23-epoxylanosta-8,24-diene[16] and methyl 3β-hydroxylanosta-8,24-dien-21-oate[11] must be erroneous, otherwise there is good agreement between the ΔM values for members of the class. Class D presents an uncertain picture with respect to the ΔM_2 values.

4. *Group* 4 ($\Delta^{9(11)}$ compounds). The two known members of Class A with fernane-type skeleton present a rather uncertain picture, unlike Class C, with lanostane skeleton, in which all the ΔM values are of the same order of magnitude. The $[\alpha]_D$ data for 3α-hydroxylanosta-9(11)-en-26,23-olide are questionable in view of its ΔM_2 value which is at variance with the observed trend (discussed above) in the sign of ΔM_2 for this group of compounds.

5. *Group* 5 ($\Delta^{7,9(11)}$ dienes). With the exception of compound (61), all the ΔM (especially ΔM_1) values for members of Class A are in good agreement. Though the two sets of values for the two members of Class B are at variance, ΔM_1 for bauradienol[11] is questionable in view of the observed trend (discussed above) in the sign of ΔM_1 for all classes of compounds with C-3β-hydroxyl.

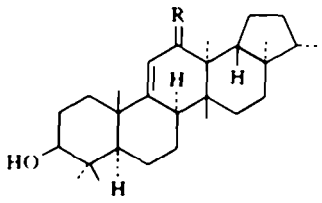
6. *Group* 6 (Δ^{12}, $\Delta^{13(18)}$ compounds). This group corresponds to the Barton and Jones' α- and β-amyrin group, but it is now subdivided into Classes A and B, according to the configuration at C-3. The data clearly confirm the earlier observation of these authors that ΔM_1 for Class A is practically negligible; this property being apparently diagnostic for the structural type in lieu of any noticeable trend in their ΔM_2 values which certainly need re-examination. The data on 3β-hydroxyolean-13(18)-ene[11] need revision.

7. *Group* 7 (Δ^{14} compounds). The data on methyl 3β-hydroxyolean-14-en-28-oate[24] call for revision. As would be expected, the ΔM values of 3β-hydroxy-13,14-cyclopropylursane agree well with those of 3β-hydroxyurs-14-ene and 3β-hydroxyolean-14-ene. The specific rotation of 3α-hydroxyolean-14-ene has been much in dispute.[21,24] The definitive value of −11.6 last recorded[23] and supported by other physico-chemical evedences gives a more acceptable ΔM_1 value in the light of the general trends herein observed.

8. *Group* 8 (compounds with C=C in ring E or ring E side chain). This group corresponds to the lupeol-betulin group of Barton and Jones,[1] but now expanded to include other compounds hitherto placed in a different group, undoubtedly due to unavailability of necessary data. Of all the structural types studied in this work, the Class A of this group provides the best

GROUP 4

Class A

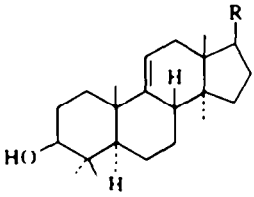


42: R = H$_2$
43a: R = H (α-OAc)

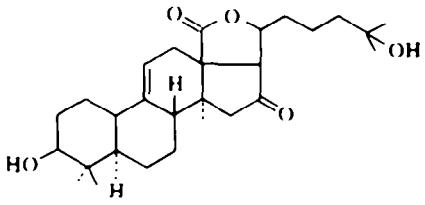
Class B

43b: C-3-epimer of 42

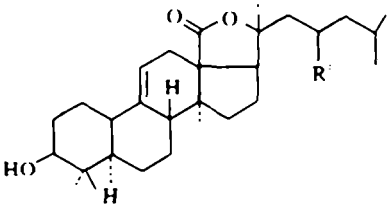
Class C



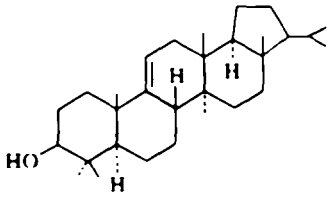
44: R = CH(CH$_3$)(CH$_2$)$_2$CH=C(CH$_3$)$_2$
45: R = CH(CH$_3$)(CH$_2$)$_3$CH(CH$_3$)$_2$
46: R = CH(CH$_3$)(CH$_2$)$_2$C(CH$_3$)$_2$C(=CH$_2$)CH$_3$
47: R = CH(CH$_3$)(CH$_2$)$_2$COOCH$_3$



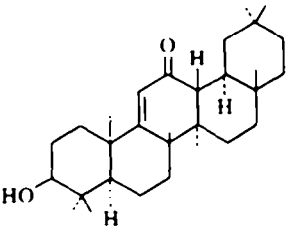
48



49: R^1 = OAc **50**: R^1 = OH



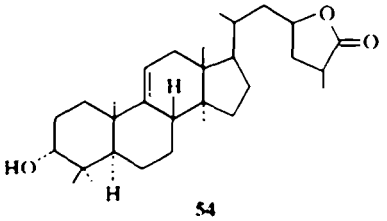
51



52

Class D

53: C-3-epimer of 51



54

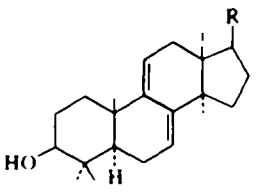
agreement in both ΔM values over a wide range of compounds. The specific rotations recorded for 3β-hydroxyhop-28-ene[17a] and dimethyl 3β-hydroxylup-20(29)-en-27,28-dioate[17b] in Class A and those of 3α-hydroxyolean-18-ene[11] in Class B are therefore obviously erroneous.

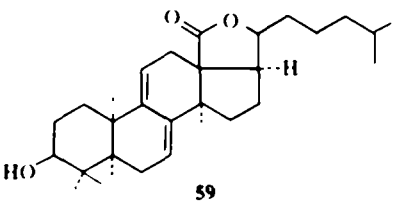
CONCLUSION

The Barton and Jones' Method of Molecular Rotation Differences (MRD) is a powerful structural tool in the field of triterpenoid chemistry whose potentiality has not been fully exploited. Since the publication of Djerassi's paper[25] in 1963, mass spectroscopy has remained the most powerful tool for the elucidation of the skeleton and, in particular, the location of C=C in pentacyclic triterpenoids. The technique of ORD and its compliment circular dichroism, which are in some ways an extension of the MRD method, have also been extensively used[26] in the solution of structural and stereochemical problems in triterpene chemistry. Unfortunately, mass spectroscopy

GROUP 5

Class A

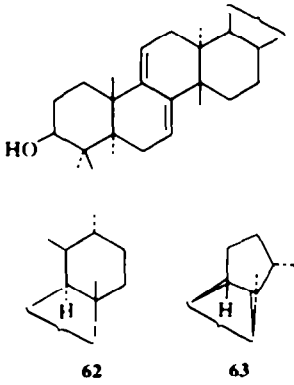




59

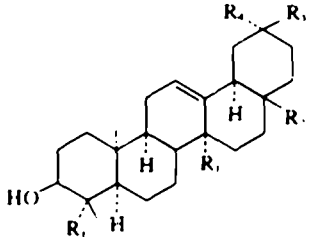
55: R = $CH(CH_3)(CH_2)_2CH{=}C(CH_3)_2$
56: R = $CH(CH_3)(CH_2)_3CH(CH_3)_2$
58: R = $CH(COOCH_3)(CH_2)_2C(=CH_2)CH(CH_3)_2$
60: R = $CH(CH_2OH)(CH_2)_2CH{=}C(CH_3)_2$
61: R = $CH(COOCH_3)(CH_2)_2CH{=}C(CH_3)_2$

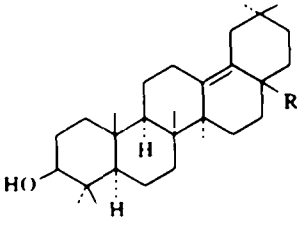
Class B



62 63

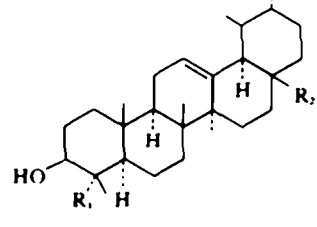
GROUP 6



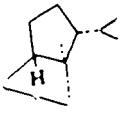


64: R_1 $R_2 = R_3 - R_4 - CH_3$
65: R_1 $R_4 = R_4 - CH_3$, R_2 - $COOCH_3$
66: R_1 - $R_2 = R_4$ - CH_3, R_3 - $COOCH_3$, 11-oxo, 18β-H
67: $R_1 - R_3 = CH_3$, $R_2 = R_4 - COOCH_3$
68: R_1 $R_4 = CH_3$, $R_2 = R_3$ - $COOCH_3$, 18β-H
69: $R_1 = R_3 - R_4 = CH_3$, Δ^{11}
70: $R_1 = R_2$ $R_4 = CH_3$, $R_3 = COOCH_3$, 11-oxo
71: $R_1 - R_2 = COOCH_3$, $R_3 - R_4 = CH_3$, 18β-H

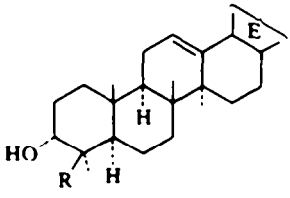
72: R - H, 16-oxo
73: R - CH_3

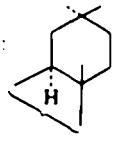


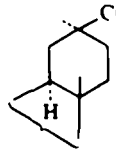
74: $R_1 = R_2 - CH_3$
75: $R_1 - COOCH_3$, $R_2 = CH_3$
76: $R_1 - CH_3$, $R_2 - COOCH_3$
77: $R_1 = R_2 = CH_3$, ring E =

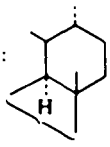


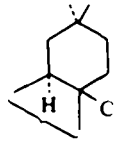
Class B



78:  , R = $COOCH_3$

80:  , R = CH_3

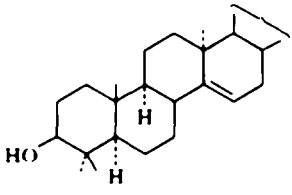
79:  , R = $COOCH_3$

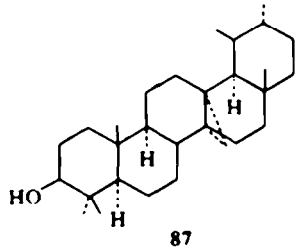
82:  , R = CH_3

81: C-3-epimer of 74

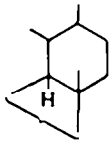
GROUP 7

Class A

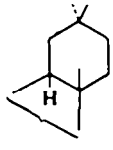




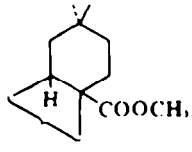
87



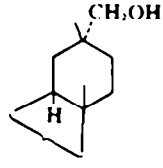
83



84



85



86

Class B

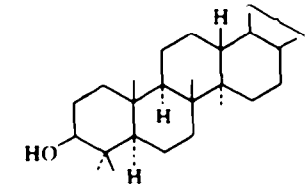
88: C-3-epimer of 84

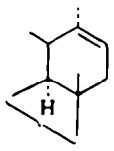
is still unable to differentiate between stereoismeric skeletons. For example, 3β-hydroxyfern-9-ene and 3β-hydroxyarbor-9-ene on the one hand,[27] and their methyl ethers on the other[6] give virtually identical mass spectra. However, the MRD method, apart from providing a relatively cheap and quick means of assigning basic stereoskeleton, locating C=C and fixing the configuration at C-3, should be able to distinguish easily between stereoisomeric skeletons. Consequently as more reliable optical rotations data on a wide range of structures become available, it will be easier to fix more precise values of MRD for various structural types with only slight stereochemical differences perhaps extending to ring E of pentacyclic triterpenoids. This will no doubt broaden the scope of the application of this method especially as electronic polarimeters, which can handle milligrams of material, are now readily available.

Finally it is pertinent to re-emphasise the most likely factor which has so far limited the general applicability of the MRD method. With spectroscopic techniques like infra-red, ultraviolet, nuclear magnetic resonance and mass spectroscopy, very valuable information can be obtained on crude specimens of compounds. However with the MRD method, this is not so. For MRD data to be useful, it is absolutely essential that optical rotation data be accurately determined on pure specimens of compounds, preferably analytical samples. The discrepancies in the data commonly found in the literature most likely to arise from a failure to recognise and appreciate these facts.

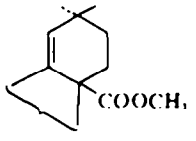
GROUP 8

Class A

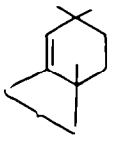




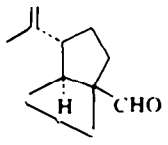
89



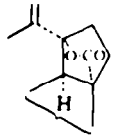
90



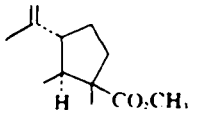
91



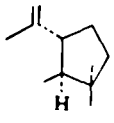
92



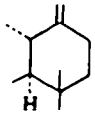
93



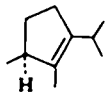
94



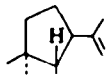
95



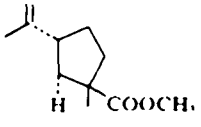
96



97

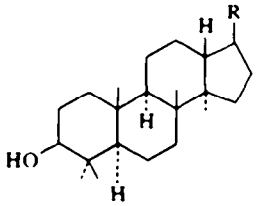


98



99

, C-14-COOCH₃



100: R = C(CH₂)(OH)(CH₂)₂CH=C(CH₃)₂

101: R = C(CH₃)(OH)(CH₂)₂CH=C(CH₃)₂

Class B

102: C-3-epimer of 98
103: C-3-epimer of 95
104: C-3-epimer of 94
105: C-3-epimer of 91

In a continuation of this work, efforts will be made to correct as many as possible of the erroneous cases, and to fill in the many gaps in the tables.

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