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Validation of Structures of Novel Eudesmane Sesquiterpenes Using Scatter Plots

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Aim: This study explores the potential of scatter plots as a tool in validating proposed structures for novel Eudesmane Sesquiterpenes.
Methodology: Substituents on the skeletons of several Eudesmane compounds were coded and plotted against the ^{13}C chemical shift values for each Carbon position on the skeleton (C_1-C_{15}).
Results: The range of chemical shift values (for each Carbon position) over which each substituent type may be obtained was determined from the scatter plots. The results imply that when the carbon atom C_1 on a novel eudesmane compound is assigned any chemical shift value between 26.1 and 54.0, then that position should definitely be without a substituent. Chemical shift values between 68.1 and 91.3 (on C_1) would indicate that β-OH as the most likely substituent (with 23.29% probability) while values within the 121.7 – 160.4 range indicate with 100% certainty that the substituent is Δ^1. Similar conclusions can be drawn for all the chemical shift ranges for the different carbon positions.
Conclusion: These chemical shift ranges could be useful in validating proposed structures for novel Eudesmane sesquiterpenes.

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Keywords: Scatter plots; skeletons; validation; eudesmane sesquiterpenes.

1. INTRODUCTION

Sesquiterpenes are formed from countless biogenetic pathways and therefore produce several types of carbon skeletons. This makes the elucidation of their structures very challenging. The biological activities exhibited by sesquiterpenes (including compounds that are insect growth regulators, antifeedant, antifungal, antitumor, antibacterials) makes relating their structures to function even more imperative. The current study focuses on Eudesmane-type compounds which are one of the most representative skeletons of sesquiterpenes. This class of compounds has been the subject of numerous phytochemical, pharmacological and synthetic studies [1-2].

The structure of any natural product is conventionally divisible into three sub-units: (i) the skeletal atoms; (ii) heteroatoms directly bonded to the skeletal atoms or unsaturations between them; and (iii) secondary carbon chains, usually bound to a skeletal atom through an ester or ether linkage [3]. Procedures that could be employed for the identification of the skeleton and substructures present in a compound have been previously described [4-7]. Artificial Neural Networks (ANNs) methods have been reported to give fast and accurate results for identification of skeletons and for assigning unknown compounds among distinct fingerprints (skeletons) of aporphine alkaloids [8]. In a previous work, we have shown that Generalized Regression Neural Networks (GRNN) could predict substituents types and positions on Eudesmane-type sesquiterpenes [9]. When the chemical shift values proposed for each of the fifteen (15) Carbon positions on the Eudesmane skeleton is used as input for the GRNN, this procedure could be used in validating the structures of novel Eudesmanes. In the current work, we use scatter plots to determine the ^{13}C chemical shift ranges (for the 15 carbon atoms on the Eudesmane sesquiterpene skeleton-shown in Fig. 1) over which different substituent types may exist. We discuss its potential application in validating structures proposed for natural products using Eudesmane sequiterpenes as reference.

2. METHODOLOGY

The structural (skeletal) ^{13}C data, substituents and stereochemical information of 325 compounds (out of 350 compounds) reviewed and published by Olievera et al. [1] was used in this study. Twenty-five of these compounds were left out owing to their structural complexity. This information can be extracted from data of Eudesmane sesquiterpenes published in literature by isolating ^{13}C values of the skeletal (carbons) from those of the substituents.

Each substituent type (on first encounter) was assigned 3 number codes. These codes serve to identify the substituent while also taking into account its possible stereochemistry (α or β) in various positions of the skeletons in other compounds.

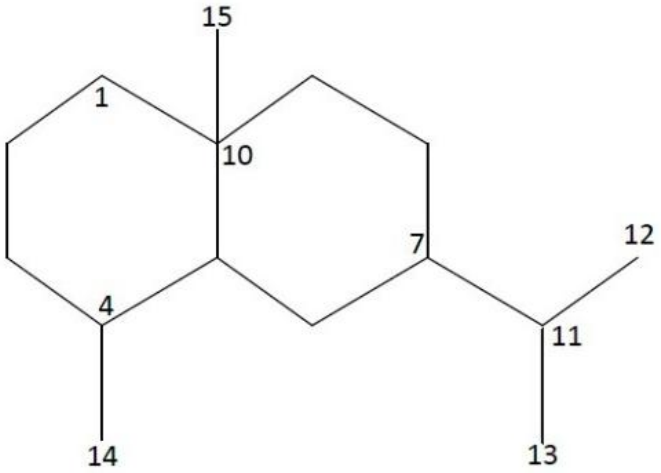


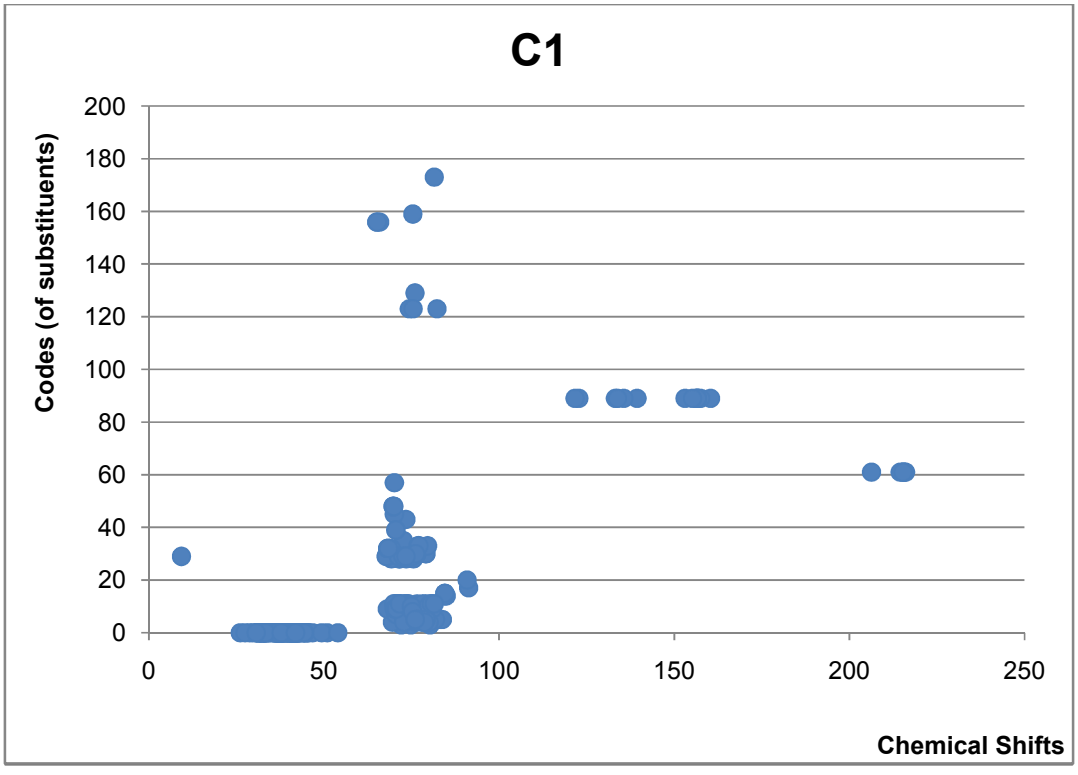
Fig. 1. The eudesmane skeleton

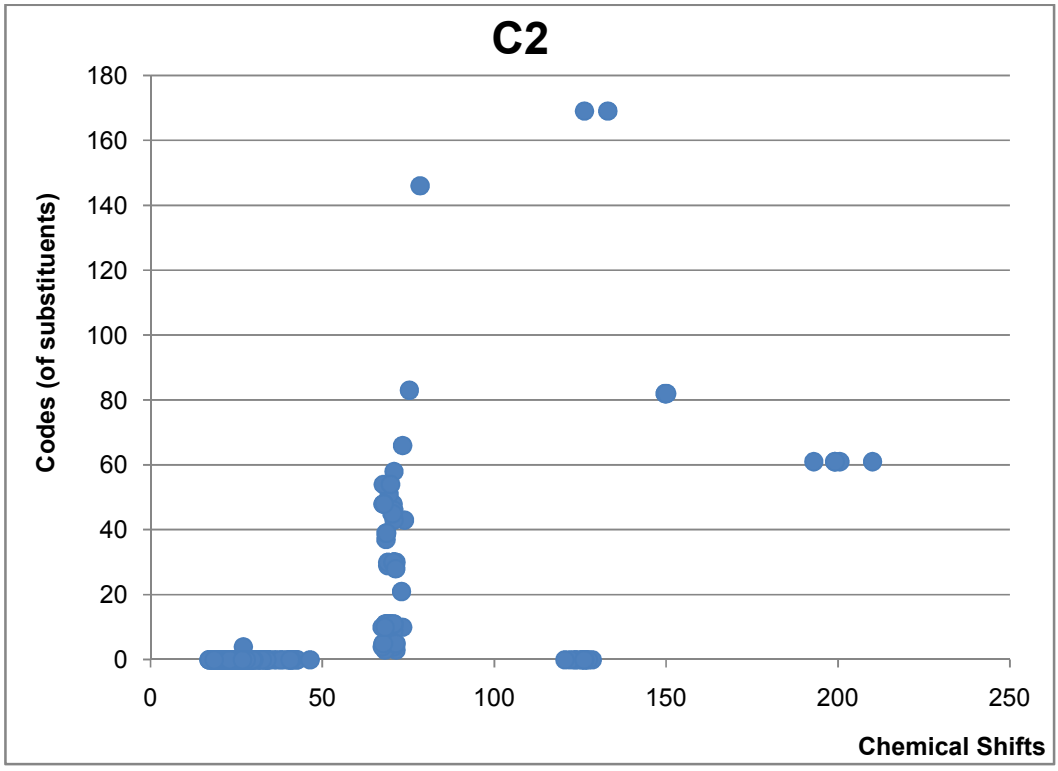
Carbon positions without substituents were assigned a code of 0 while α and β positions without substituent(s) were assigned codes of 1 and 2 respectively. For example, OH group was given a code of 3, an α-OH is given a code of 4 while a β-OH was assigned a code of 5. (The different substituent types and the corresponding codes assigned to them are shown in Appendix 1). Thereafter, 30 columns containing, alternately, all the possible ^{13}C chemical shift data for each of the 15 positions (C_1-C_{15}) on the Eudesmane skeleton for all the 325 compounds and the corresponding codes for the substituents attached to each position in each of the compounds, were prepared on an Excel sheet. A scatter plot of the codes (of the substituents) against the ^{13}C chemical shift values for each Carbon position on the skeleton (C_1-C_{15}) was plotted. From this, the range of chemical shift values (for each Carbon position) over each substituent type may be obtained was determined. Where there are multiple possible substituent types within a particular carbon range, the probability (in percentages) that a substituent would occupy this position was determined relative to the total number of points within the range.

3. RESULTS AND DISCUSSION

Fig. 2 shows the scatter plots of codes of substituents against their corresponding chemical shift values. From this, the chemical shift ranges characteristic of each substituent type on each of the fifteen (15) carbon atoms on the Eudesmane skeleton was obtained.

Scatter plots (in conjunction with other CASE procedures) have previously been used by Elyashberg et al. [10] in the revision of the structure of Asperjinone. The authors performed a search for the (3,3-dimethyloxiran-2-yl) methyl fragment in the ACD/NMR Database containing 425,000 structures with assigned ^{13}C and ^{1}H chemical shifts. The program selected 180 structures of which about 150 structures exhibiting the closest similarity with the environment of the oxirane fragment were chosen. For these structures, a scatter plot was created. Inspection of the scatter plot convincingly confirms the incorrectness of the original structure.




C2
Codes (of substituents)
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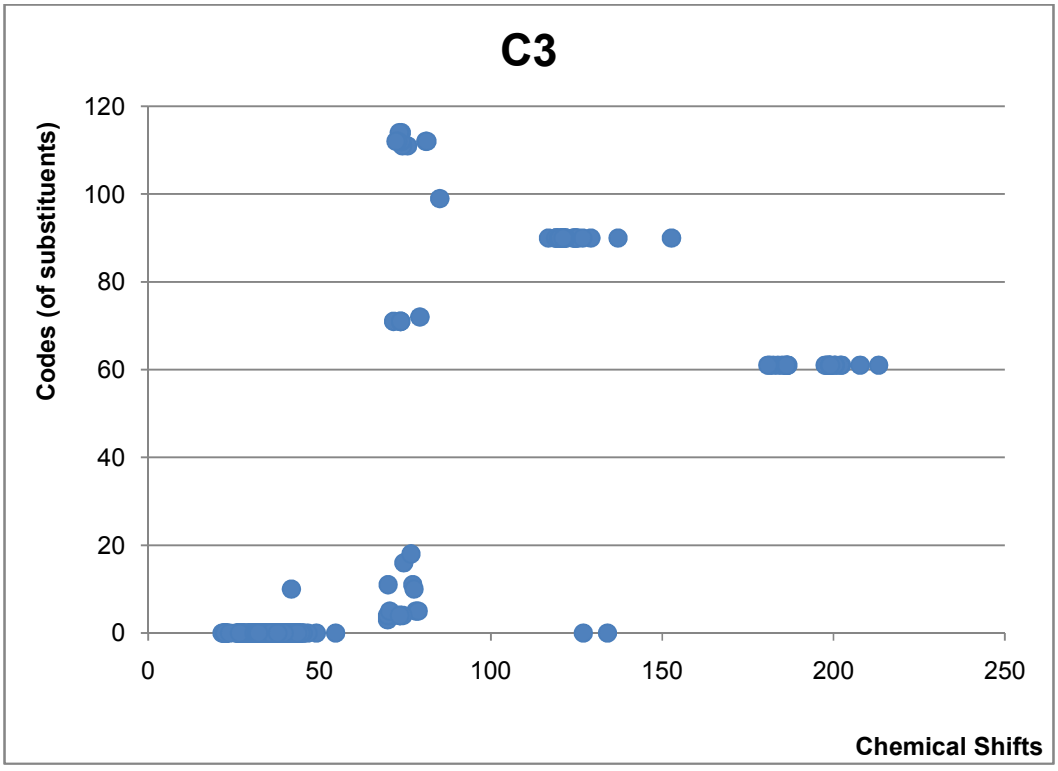
160
140
120
100
80
60
40
20
0
0
50
100
150
200
250
Chemical Shifts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Codes (of substituents)
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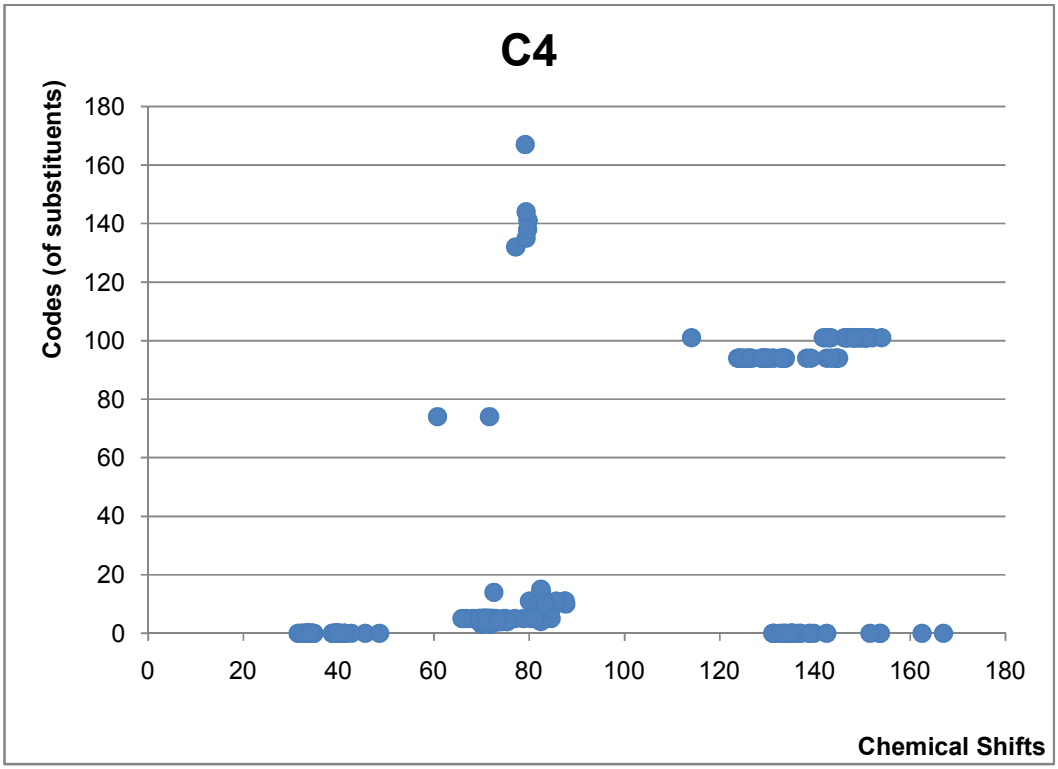
20
0
0
50
100
150
200
250
Chemical Shifts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Codes (of substituents)
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0
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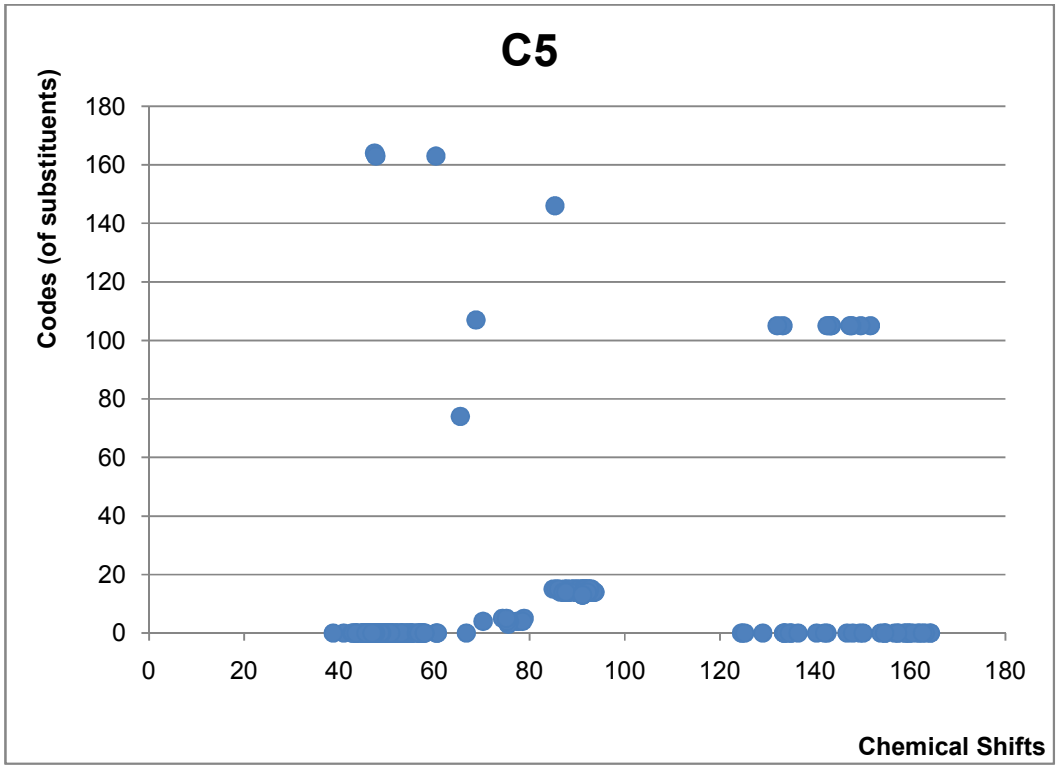
100
120
140
160
180
Chemical Shifts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100
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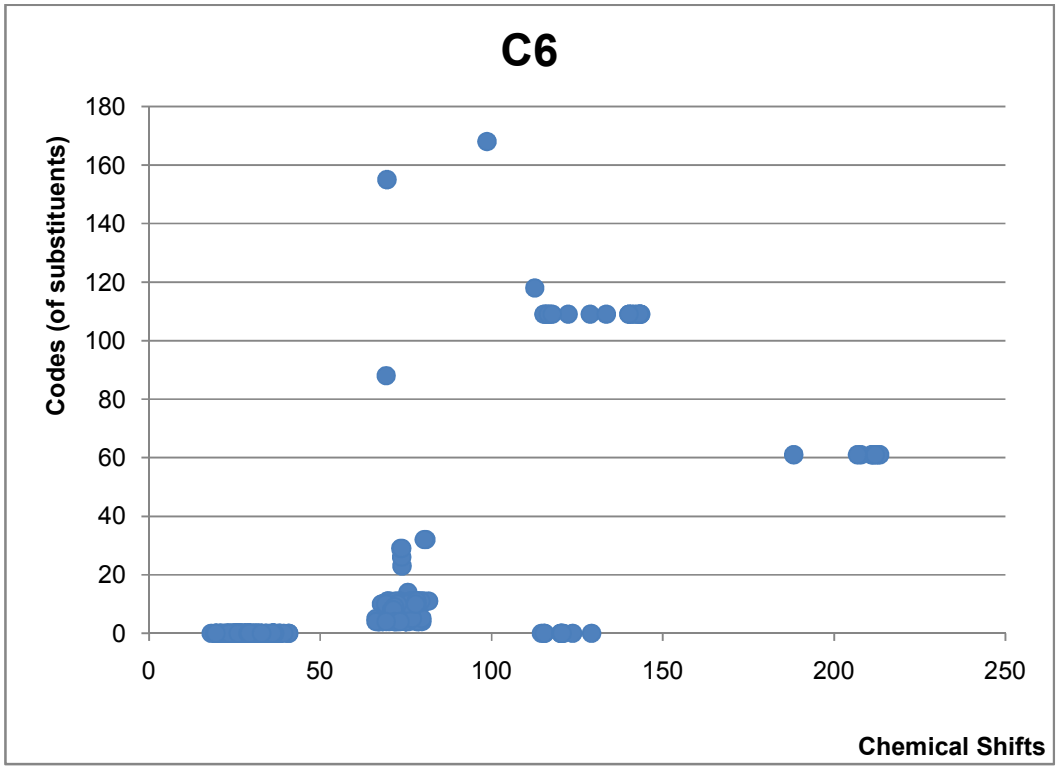
140
160
180
Chemical Shifts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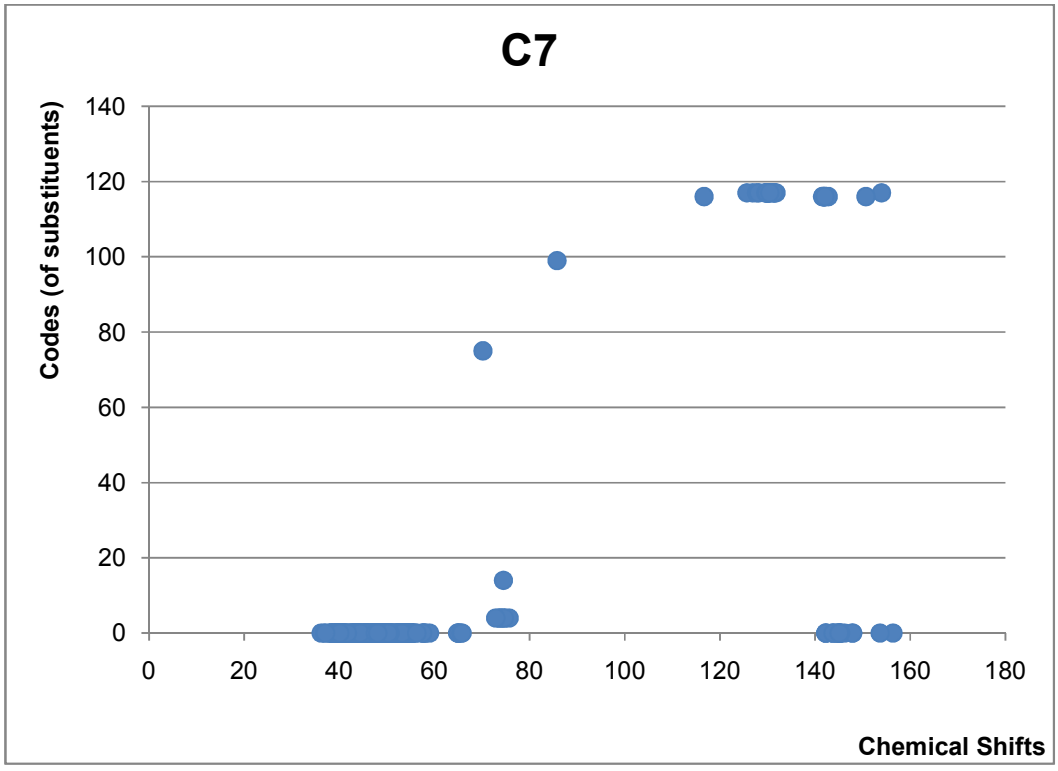
250
Chemical Shifts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Codes (of substituents)
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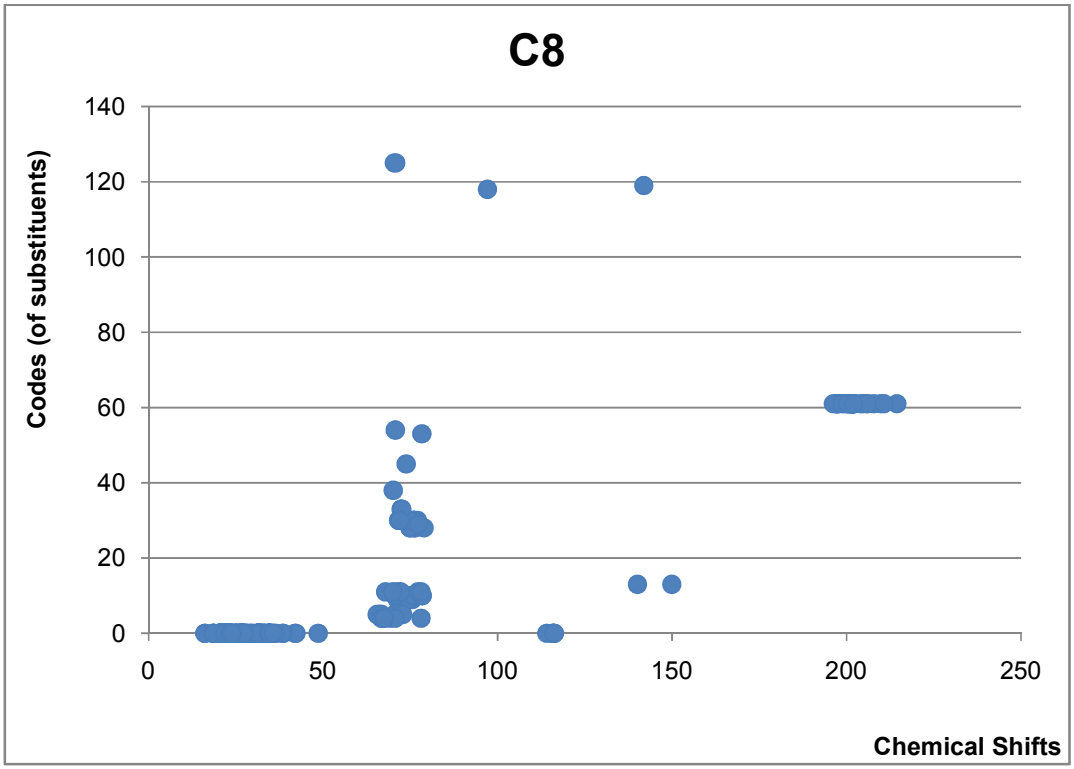
140
160
180
Chemical Shifts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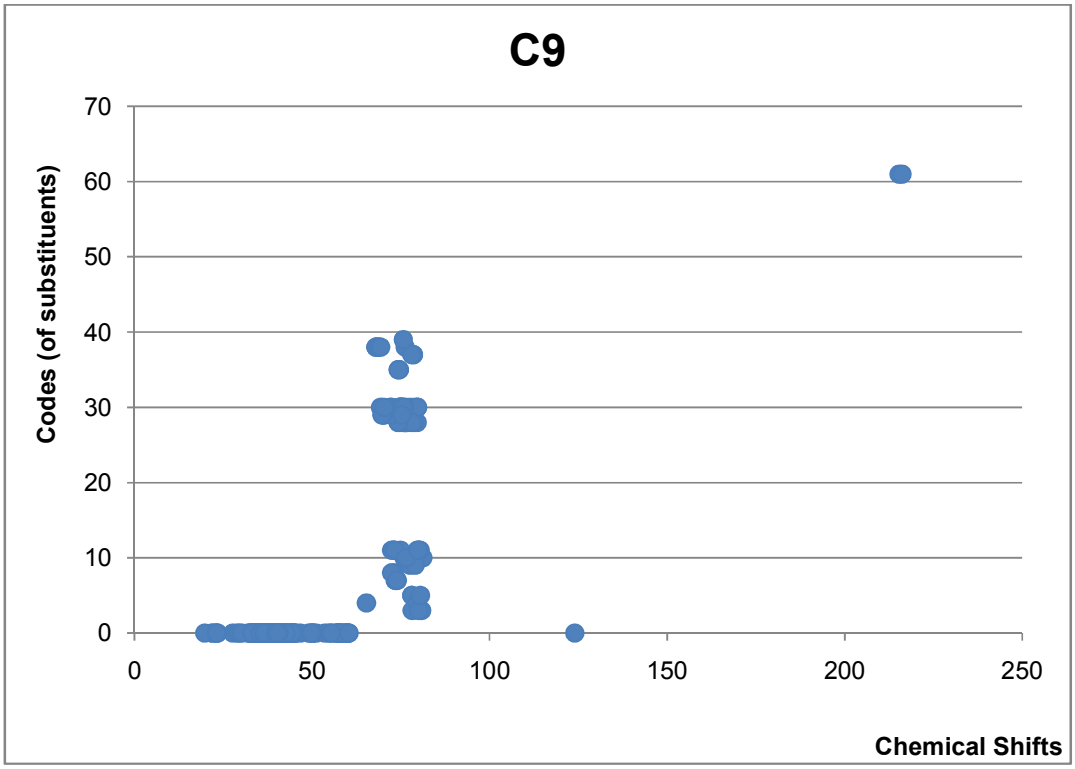
250
Chemical Shifts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0
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100
150
200
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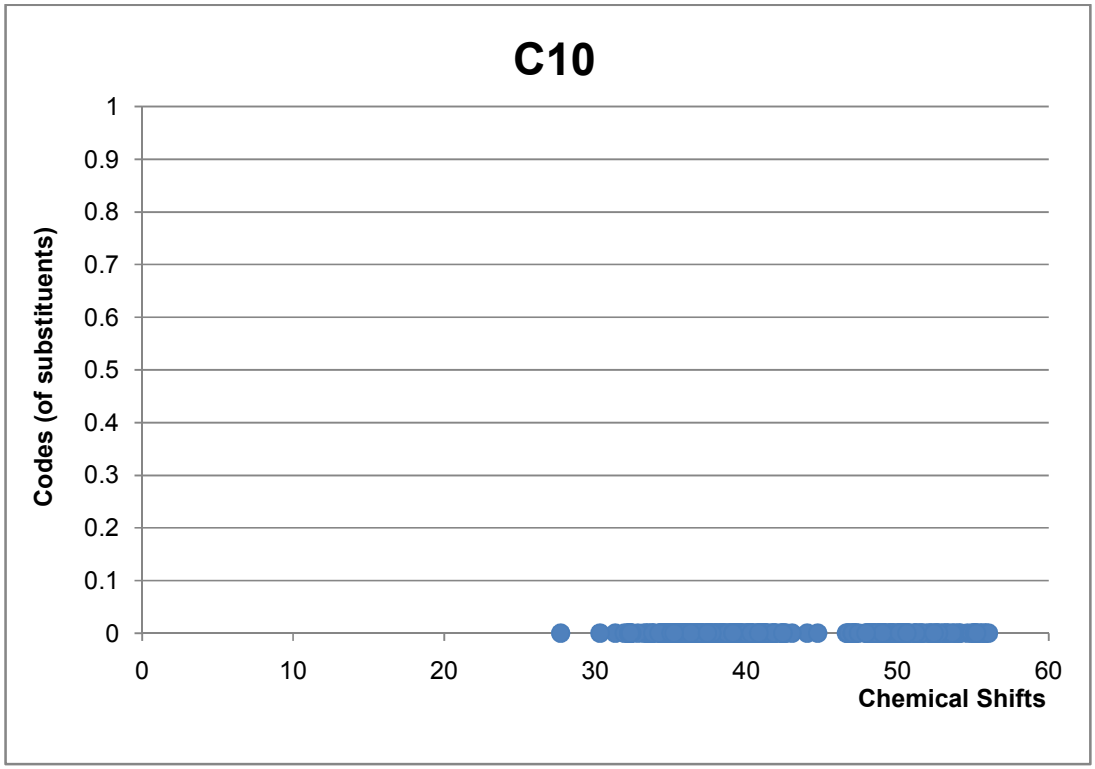
Chemical Shifts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Codes (of substituents)
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0.2
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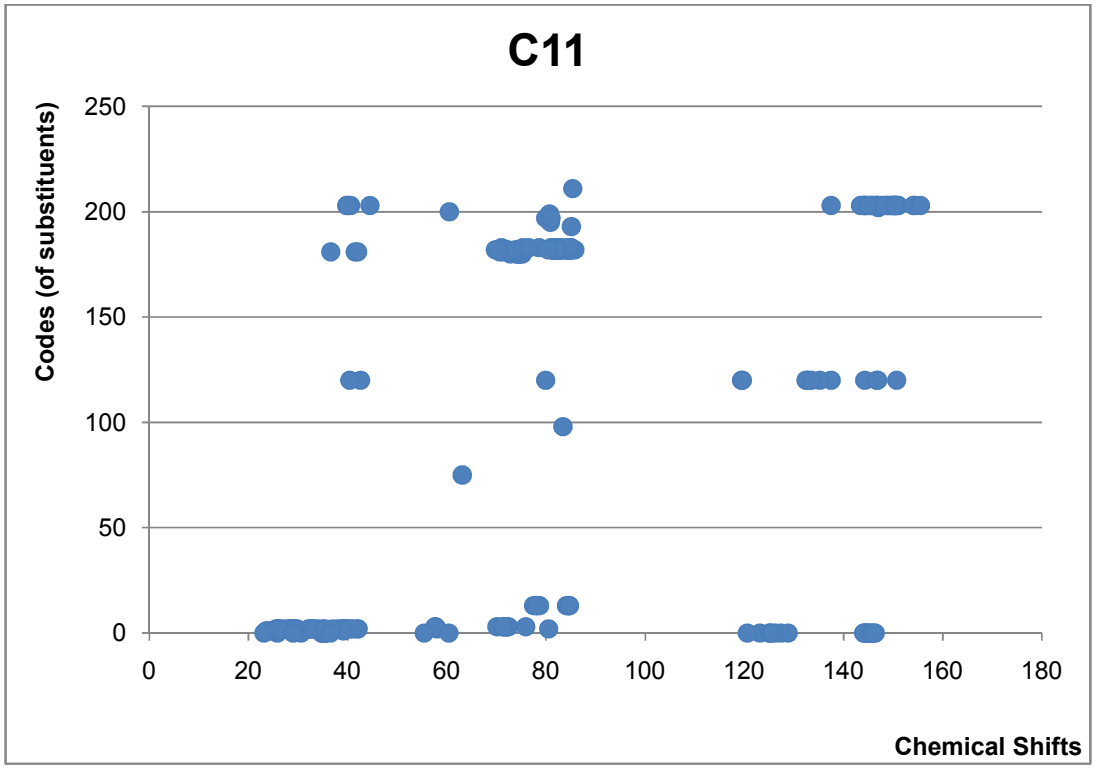
0
0
10
20
30
40
50
60
Chemical Shifts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Codes (of substituents)
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200
150
100
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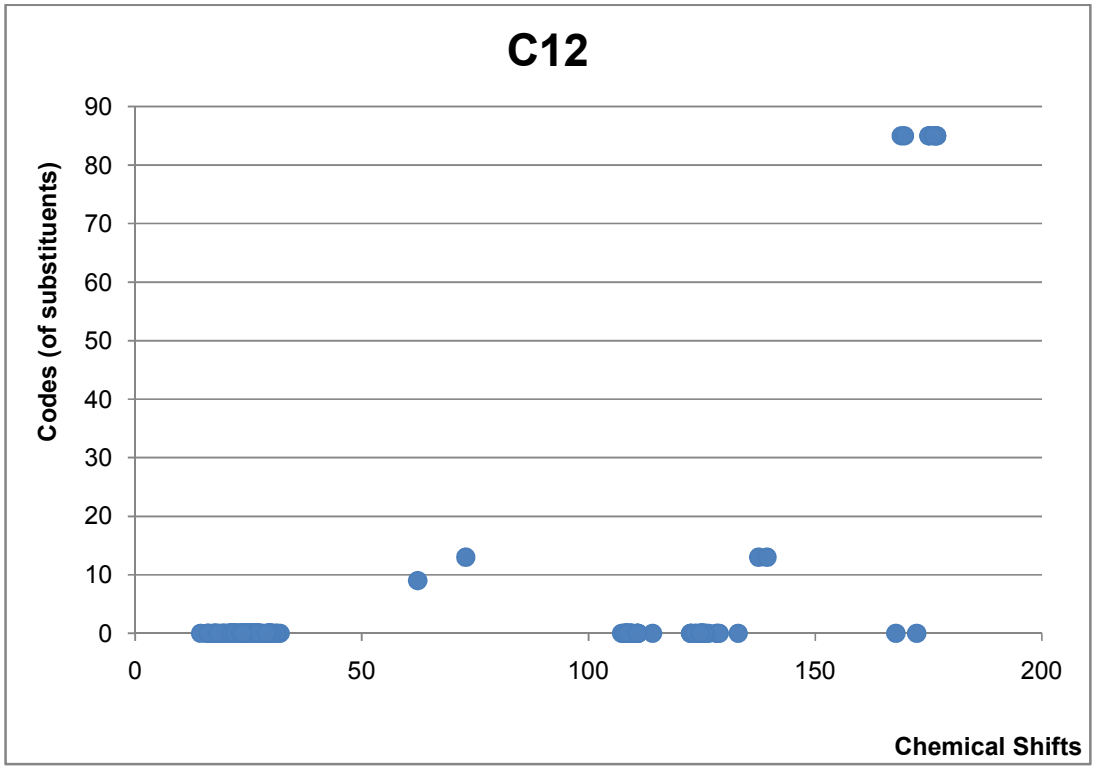
0
0
20
40
60
80
100
120
140
160
180
Chemical Shifts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Codes (of substituents)
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60
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40
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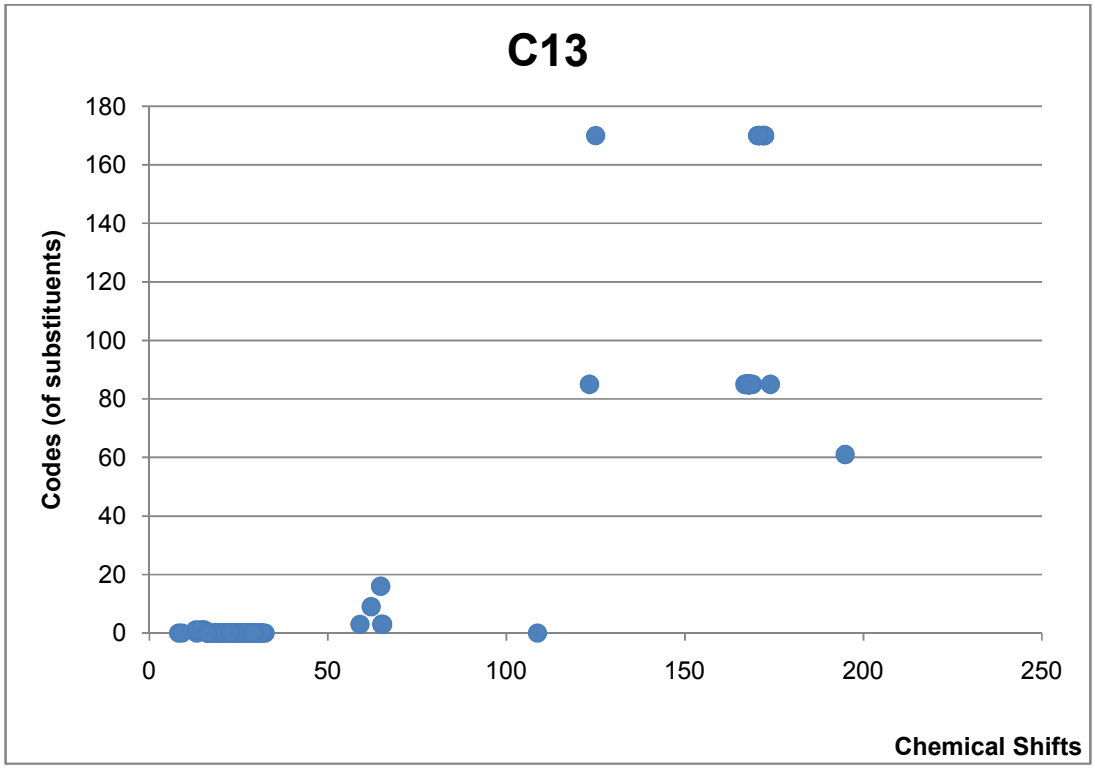
Chemical Shifts


C13
Codes (of substituents)
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140
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100
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40
20
0
0
50
100
150
200
250
Chemical Shifts

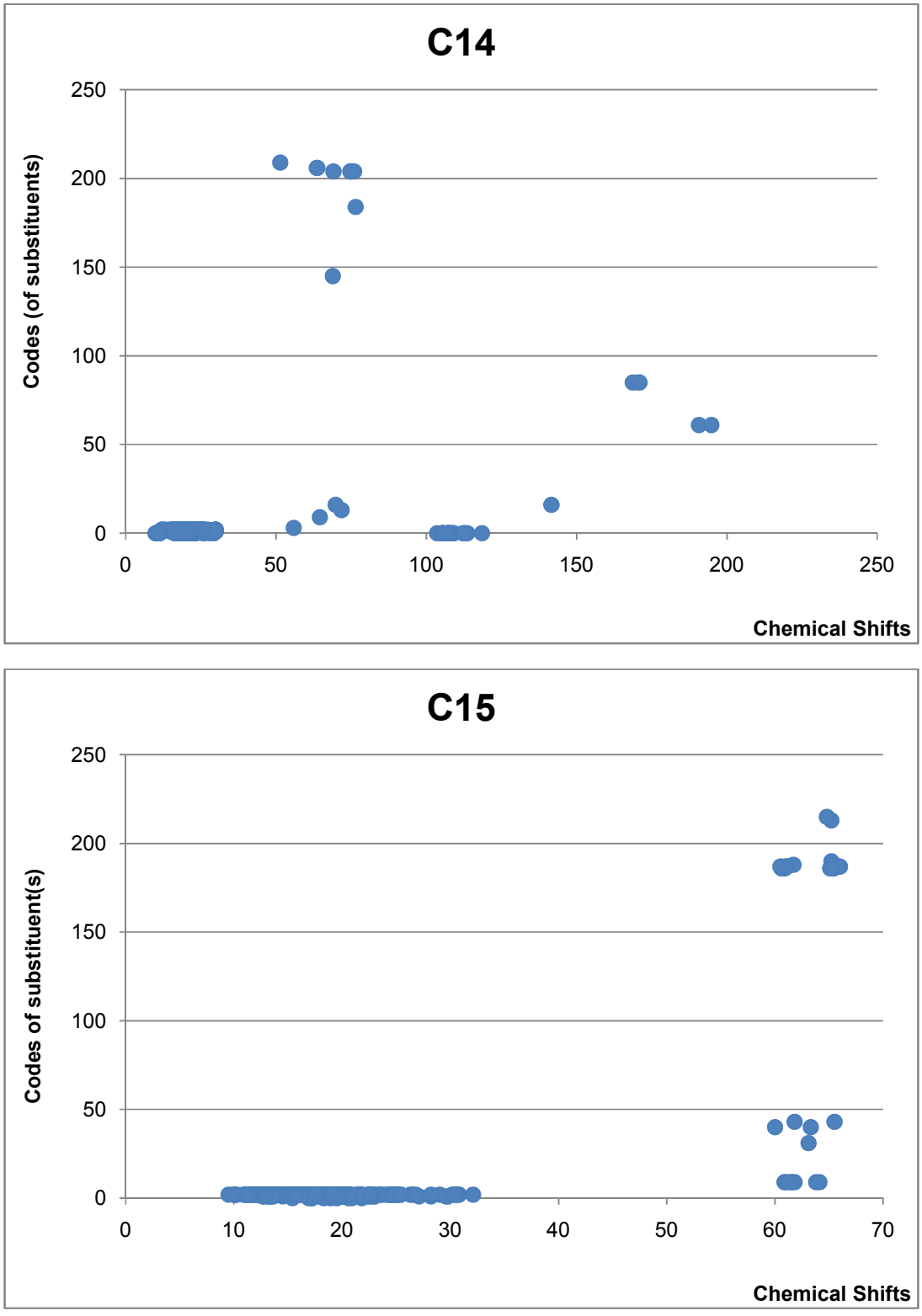

Fig. 2. Scatter plots of codes (of substituents) against ^{13}C chemical shifts

Oliveira et al. [1] described the use of two component programs (TIPCARB and PICKUP) of the system, SISTEMAT, in the search for heuristic rules (practical rules obtained from the experience of specialists, or originated from programs which perform "learning from machine" routines, and are aimed at solving a specific problem). TIPCARB can determine which carbon atom is present in each position on a skeleton whether or not a carbon atom is substituted and the kind of substituent. After the position and types of substituents attached to each carbon atom have been defined, the fragments, denominated substructures, are coded in the PICKUP program that performs the search of the database for the chemical shift range for ^{13}C data of the carbons in the substructure. The authors then utilized the PICKUP program to determine several chemical shift ranges that characterize several substructures present in eudesmanes. A summary of the substituent types that may be obtained over different ^{13}C ranges for each of the fifteen (15) positions on the Eudesmane skeleton using scatter plots are presented in Table 1.

Table 1. Chemical shift ranges for substituents on the eudesmane skeleton

Skeletal carbon	Chemical shift range	Codes of substituents (%)
C_1	26.1 - 54.0	Nil(100)
	68.1- 91.3	OH(2.74), α-OH(4.11), β-OH(23.29), α-Ocin(2.05), β-Ocin(2.05), OAc(13.70), α-OAc(3.42), β-OAc(13.01),α-Oxy(1.37), β-Oxy(0.68), α- OGly(0.68), α-OGly $(OAc)_4$ (0.68), OBzt(3.42), α-OBzt(8.22), β-O Bzt (5.48), α-ONic(2.74), β-ONic (2.05), α-OEpcin(0.68), β-OFur(1.37), OiBu(0.68), β-OiBu(0.68), β-OBut(2.05), β-O2MeBu(0.68), β-O(α-OH–Dihydrocou)-2.05, β-O(α-OH–Iva)-0.68, OPro(0.68), β-O(Val-2'OH)-0.68
	121.7 - 160.4	Δ^1(100)
	206.3 - 216	Oxo(100)
C_2	17.0 - 46.4	Nil(100)
	67.4 -78.4	OH(3.45), α-OH(6.90), β-OH(10.34) , OAc(5.17), α-OAc(8.62), β-OAc(15.52), β-OGly$(oac)_4$ (1.72), OBzt(1.72), α-OBzt(1.72), β-OBzt (10.34), OFur(1.72), α-OFur(1.72) β-OFur(3.45), OiBu(3.45), β-OiBu (3.45), OBut(1.72), β-OBut(8.62), β-OBut –(2'-Me)-1.72, β-OMeBu(3.45), OHex(1.72), β- OGly-(2'6'-OAc)-1.72, α-OMe(1.72), α-Peroxy(1.72)
	120.5–128.5; 126.2-133	Nil(minor) Δ^2(minor)
	192.1 - 210	Oxo
C_3	21.6 - 54.7	Nil(100)
	69.9 -85.1	OH(3.45), α-OH(17.24), β-OH(10.34), α-OAc(3.45), β-OAc (6.90), OGly(3.45), β-OGly(3.45), α-OEpang(10.34), β-OEpang(3.45), α-OOH(3.45), α-OAng(6.90), β-OAng(20.69), α-O 2MeBu-(2'OAc,3'OH)(6.90)
	127.0– 134.0 116.8-152.7	Nil(12.5) Δ^3(87.5)
	180.8 – 213.1	Oxo(Nil)
C_4	31.5 – 48.6	Nil(100)
	65.9– 87.7	OH(4.17), α-OH(29.17), β-OH(37.5), β-OCin(4.17), α-OAc(8.33), β-OAc(4.17), α-Oxy(3.13), β-Oxy(1.04), α-Epoxy(2.08), β-OFuc(1.04), β-OFuc(2'OMeBu)-1.04, β-OFuc$(OAc)_3$-1.04, β-O Fuc(2'OMeBu,3'4'OAc)(1.04), β-OFuc(3'4'-oisopropylidene)-1.04, β-OFuc(2'OMeBu,3'4'-isopropylidene)-1.04
	123.8 – 167.0	Nil(27.59), Δ^4(40.23), $\Delta^{4(14)}$(32.18)

Skeletal carbon	Chemical shift range	Codes of substituents (%)
C_5	38.7 – 60.6	Nil(97.7), α-H(1.15), β-H(1.15)
	66.7 – 78.8	Nil(6.67), OH(6.67), α-OH(53.33), β-OH(20), α-Epoxy(6.67), α-NC(6.67)
	84.9 – 93.7	Oxy(1.72), α-Oxy(62), β-Oxy(35), α-Peroxy(1.72)
	124.5 – 164.2	Nil(78.05), Δ^5(21.95)
C_6	18.2 – 40.9	Nil(100)
	66.3 – 80.9	α-OH(19.54), β-OH (4.60), OCin(3.45), β-OCin (9.20), OAc(3.45), α-OAc(31.03), β- OAc(20.69), α-Oxy(1.15), α-Otrans-(3'-OAc-2-butenoate)(1.15), α-OCis-(3'-OAc-2-butenoate)(1.15), α-OBzt(1.15), α-ONic(1.15), β-Otrans-cou(1.15), βCin(1.15)
	112.6 – 143.6	OBzt(28), Δ^6 (68), β-OH, α-Oxy(4)
	207.8 – 213.3	Oxo(100)
C_7	36.2 – 65.8	Nil(100)
	70.2 – 85.8	α-OH(70), α-Oxy(10), β-Epoxy(10), α-OOH(10)
	125.7 – 156.4	Nil(58.54), Δ^7(14.63), $\Delta^{7(11)}$(26.82)
C_8	16.1 – 48.6	Nil(100)
	65.5 – 78.9	α-OH (10.91), β-OH(9.09), OAc(5.45), α-OAc(18.18), β-OAc(10.91), OBzt(7.27), α- OBzt (5.45), β-OBzt(18.18), β-ONic(3.64), α-OFur(1.82), β-OiBu(1.82), α-OMebu (1.53), β- OMebu(1.53), α-OMeAcr-(4'OH)(3.64)
	114.1 – 116.2	Nil
	196.2 – 214.4	Oxo
C_9	19.8 – 60.4	Nil(100)
	65.3 – 81.2	OH(3.48), α-OH(2.33), β-OH(2.33), α-OCin(4.65), β-OCin(2.33), OAc (2.33), α-OAc(5.81), β-OAc(10.47), OBzt(11.63), α-OBzt(19.77), β-OBzt(23.26), α-OEpcin(2.33), OFur(2.33), α-OFur(5.81), β-OFur (1.16)
	215.4 – 216.1	Oxo(minor)
C_{10}	27.7 – 55.8	Nil(100)
C_{11}	23.1 – 42.6	Nil(20), α(5.45), β(58.18), Δ^{11}(3.64), OH,β(5.45), Δ^{11}, β-(7.27)
	55.4 – 63.1	Nil(28.57), β(14.29), oh (28.57), β-epoxy(14.29), NC,α(14.29)
	70.1 – 85.4	β(2.17), OH(8.70), Oxy (6.52), OOH(1.09), Δ^{11} (1.09), OH, α(6.52), OH, β(1.52), Oxy,α(34.78), Oxy, β (17.39), Oxyl-$(OAc)_3$(2.17), OAra, β (1.09), OCin, β(1.09)
	119.4 – 155.5	Nil(23.44), Δ^{11}(18.75), Δ^{11},α(3.13), Δ^{11},β(54.69)
C_{12}	14.4 – 31.9	Nil(100)
	108.4 – 133.0	Nil(100)
	137.5 – 139.4	Oxy(minor)
	167.8 – 176.4	Nil(28.57), Oxo, OMe(71.43)
C_{13}	8.2 – 32.4	Nil (94.85), α(5.15)
	59.0 – 65.1	OH(50), OAc(25), OGly(25)
	167.0 - 174	Oxo,OMe(56.25), Oxo, OH(43.75)
C_{14}	9.9 – 29.9	Nil(24.1), α(31.93), β(43.98)
	51.4 – 76.5	OH(9.09), OAc(9.09), Oxy(9.09), OGly(9.09), Peroxy(9.09), Oxy, α(9.09), OGly, α(2.73), OH,α(9.09), Epoxy, β(9.09)
	105.3 – 118.5	Nil(100)
	168.7 – 170.9	Oxo, OMe(minor)
	190.7-194.8	Oxo(minor)

Skeletal carbon	Chemical shift range	Codes of substituents (%)
C_{15}	9.5 – 32.1	Nil(5.33), α(19.53), β(75.15)
	60.0 – 66.0	OAc(21.21), Oxy(3.03), OPic(6.06), OiBu(6.06), OAc, α(18.18), OAc, β(30.30), OiBu,α(6.06), OMeBu, α(3.03), α-OH, β(3.03), α-OAc, β(3.03)

From the Table, it can be inferred, for example that when the carbon atom on position 1 (C_1) on a novel eudesmane compound is assigned any chemical shift value between 26.1 and 54.0, then that position should definitely be without a substituent. Chemical shift values between 68.1 and 91.3 would indicate that β-OH as the most likely substituent (with 23.29% probability) while other substituents shown on the Table would have lesser probabilities of occurrence. Chemical shift values within the 121.7 – 160.4 range indicate with 100% certainty that the substituent is Δ^1. When the carbon on position 2 (C_2) on a novel eudesmane compound is assigned a chemical shift value between 17.0 and 46.4, the position is definitely without a substituent. It could be observed that when a chemical shift value between 67.4 and 78.4 is assigned to this position, all the possible substituents (listed against this position on the Table) have very similar probabilities of occupying this position. It should be noted, however, that this procedure has successfully reduced the number of likely substituents for this position from about 215 to the 22 reflecting on the Table. Again, the stereochemistry of each substituent type has been taken into consideration in assigning codes to the substituents (reflected as α or β on the Table). The user would be able to reach a conclusion (without regard to stereochemistry) that the substituents OH and OAc have 20.69% and 29.31% probabilities of occurring in this position. Similar conclusions can be drawn for all the chemical shift ranges for the different carbon positions indicated on the Table. Isolated chemical shift values were not included on the Table (for example value of 27 on scatter plot for C_2). Chemical shift ranges with very few substituent types were tagged 'minor' on the Table.

An assigned substituent to a position on the skeleton of a novel Eudesmane compound would be deemed wrong when the ^{13}C NMR chemical shift value assigned to its position on the skeleton does not fall within the correct chemical shift range obtained for that substituent type (from the scatter plot). The probability values (given in parenthesis) are an indication of the likelihood that the substituent would be found in that position on the skeleton of an unknown compound. The accuracy of the carbon ranges in validating the substituents proposed for each carbon position in an unknown eudesmane compound would depend on the degree of representativeness of their skeletal and/or substituent types among those used in plotting the graphs.

4. CONCLUSION

With the availability of sufficiently broad database on the ^{13}C chemical shift values of the carbon atoms on the Eudesmane skeleton, scatter plots may be a useful complementary tool in the elucidation of structure of this class of compounds.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Oliveira FC, Ferreira MJP, Nunez CV, Rodriguez GV, Emerenciano VP. ^{13}C NMR spectroscopy of Eudesmane Sesquiterpenes. Progress in Nuclear Magnetic Resonance Spectroscopy. 2000; 37: 1-45.
2. Ferreira MJP, Oliveira FC, Rodrigues GV, Emerenciano VP. ^{13}C NMR pattern recognition of Guaiane Sesquiterpenes. Internet Electr. J. Mol. Des. 2004;3(11): 737-749.
3. Rodrigues GV, Campos IPA, Emerenciano VP. Applications of artificial intelligence to structure determination of organic compounds**. Determination of groups attached to skeleton of natural products using 13 C nuclear magnetic resonance spectroscopy. Spectroscopy. 1997;191-200.
4. Ferreira MJP, Rodrigues GV, Brant AJC, Emerenciano VP. REGRAS: An auxiliary program for pattern recognition and substructure elucidation of monoterpenes. Spectroscopy. 2000;15:65–98.

5. Ferreira MJP, Brant AJC, Rodrigues GV, Emerenciano VP. Automatic identification of terpenoid skeletons through 13C nuclear magnetic resonance data disfunctionalization. Analytica Chimica Acta. 2001;429:151–170.

6. Ferreira MJP, Oliveira FC, Alvarenga SAV, Macari PAT, Rodrigues GV, Emerenciano VP. Automatic identification by 13C NMR of substituent groups bonded in natural product skeletons. Computers & Chemistry. 2002;26:601–632.

7. Ferreiraa MJP, Emerenciano VP, Linia GAR, Romoff P, Macarib PAT, Rodrigues GV. ^{13}C NMR spectroscopy of monoterpenoids. Progress in Nuclear Magnetic Resonance Spectroscopy. 1998; 33:153–206.

8. Rufino AA, Brant AJC, Santos JBO, Ferreira MJP, Emerenciano VP. Simple method for identification of aporphine alkaloids from ^{13}C NMR data using artificial neural networks. J. Chem. Inf. Model. 2005;45:645-651.

9. Alawode TT, Alawode KO. Prediction of substituent types and positions on skeleton of Eudesmane-type sesquiterpenes using generalized regression neural networks. African Journal of Pure and Applied Chemistry. 2014;8(7):102-109.

10. Elyashberg M, Blinov K, Molodstov S, Williams AJ. Structure Revision of Asperjinone Using Computer-Assisted Structure Elucidation Methods. Journal of Natural Products. 2013;76(1):113-116.

APPENDIX

Appendix 1. Substituents and their corresponding codes

Substituent	Code	Substituent	Code	Substituent	Code	Substituent	Code
Nil	0	α-O-cis-(3'-OAc-2-butenoate)	26	β-OBut-(2'-Me)	51	4-O(CH_2)O-4	76
α	1	β-O-cis-(3'-OAc-2-butenoate)	27	OMeBu	52	α-4-O(CH_2)O-4	77
β	2	OBzt	28	α-OMeBu	53	β-4-O(CH_2)O-4	78
OH	3	α-OBzt	29	β-OMeBu	54	Nor	79
α -OH	4	β-OBzt	30	O2MeBu	55	α-Nor	80
β-OH	5	ONic	31	α-O2MeBu	56	β-Nor	81
OCin	6	α-ONic	32	β-O2MeBu	57	OMe	82
α -OCin	7	β-ONic	33	OHex	58	α-OMe	83
β-OCin	8	OEpcin	34	α-OHex	59	β-OMe	84
OAc	9	α-OEpcin	35	β-OHex	60	Oxo,OMe	85
α -OAc	10	β-OEpcin	36	Oxo	61	O-trans-Cou	86
β-OAc	11	OFur	37	α-Oxo	62	α-O-trans-Cou	87
Oxy	13	α-OFur	38	β-Oxo	63	β-O-trans-Cou	88
α-Oxy	14	β-OFur	39	OGly-(2',6'-OAc)	64	Δ^1	89
β-Oxy	15	OPic	40	α-OGly-(2',6'-OAc)	65	Δ^3	90
OGly	16	α-OPic	41	β-OGly-(2',6'-OAc)	66	OGly[$(OAc)_3$6'-OTig]	91
α-OGly	17	β-OPic	42	Trinor	67	α-OGly[$(OAc)_3$6'-OTig]	92
β-OGly	18	OiBu	43	α-Trinor	68	β-OGly[$(OAc)_3$6'-OTig]	93
OGly-$(OAc)_4$	19	α-OiBu	44	β-Trinor	69	Δ^4	94
α-OGly-$(OAc)_4$	20	β-OiBu	45	OEpang	70	OXyl-$(OAc)_3$	95
β-OGly-$(OAc)_4$	21	OBut	46	α-OEpang	71	α-OXyl-$(OAc)_3$	96
O-trans-(3'-OAc-2-butenoate)	22	α-OBut	47	β-OEpang	72	β-OXyl-$(OAc)_3$	97
α-O-trans-(3'-OAc-2-butenoate)	23	β-OBut	48	Epoxy	73	OOH	98
β-O-trans-(3'-OAc-2-butenoate)	24	OBut-(2'-Me)	49	α-Epoxy	74	α-OOH	99
O-cis-(3'-OAc-2-butenoate)	25	α-OBut-(2'-Me)	50	β-Epoxy	75	β-OOH	100

Appendix 1. (Continues): Substituents and their corresponding codes

Substituent	Code	Substituent	Code	Substituent	Code	Substituent	Code
$\Delta^{4(14)}$	101	β-α-OMeAcr-(4'OH)	126	$\Delta^{5(10)}$	152	[OGly(OAc)$_3$-(2'OGly(OAc)$_4$)]	177
OAra	102	O(α-OH-iVa)	127	Cin	153	α-[OGly(OAc)$_3$-(2'OGly(OAc)$_4$)]	178
α-OAra	103	α-O(α-OH-iVa)	128	α-Cin	154	β-[OGly(OAc)$_3$-(2'OGly(OAc)$_4$)]	179
β-OAra	104	β-O(α-OH-iVa)	129	β-Cin	155	11OH, 11 α	180
Δ^5	105	OFuc	130	Br	156	11OH, 11 β	181
NC	106	α-OFuc	131	α-Br	157	11Oxy, 11 α	182
α-NC	107	β-OFuc	132	β-Br	158	11Oxy, 11 β	183
β-NC	108	OFuc-(2'OMeBu)	133	OPro	159	14Oxy, 14 α	184
Δ^6	109	α-OFuc-(2'OMeBu)	134	α-OPro	160	14Oxy, 15 β	185
OAng	110	β-OFuc-(2'OMeBu)	135	β-OPro	161	15OAc, 15 α	186
α-OAng	111	OFuc-(OAc)$_3$	136	H	162	15OAc, 15 β	187
β-OAng	112	α-OFuc-(OAc)$_3$	137	α-H	163	15OiBu,15 α	188
O2MeBu-(2'OAc,3'OH)	113	β-OFuc-(OAc)$_3$	138	β-H	164	15OiBu,15 β	189
α-O2MeBu-(2'OAc,3'OH)	114	OFuc-(2'OMeBu3'4' OAc)	139	OFuc-(2'OMeBu3'4' isopropylidene)	165	15OMeBu, 15 α	190
β-O2MeBu-(2'OAc,3'OH)	115	α-OFuc-(2'OMeBu3'4' OAc)	140	α-OFuc-(2'OMeBu3'4' isopropylidene)	166	15OMeBu, 15 β	191
Δ^7	116	β-OFuc-(2'OMeBu3'4' OAc)	141	β-OFuc-(2'OMeBu3'4' isopropylidene)	167	11OAc, 11α	192
$\Delta^{7(11)}$	117	OFuc(3'4' Oisopropylidene)	142	β-OH,α-Peroxy	168	11OAc, 11β	193
β-OH, α-Oxy	118	α-OFuc(3'4' Oisopropylidene)	143	Δ^2	169	11-OGly[(OAc)$_3$6'-OTig], 11α	194
Δ^8	119	β-OFuc(3'4' Oisopropylidene)	144	Oxo, OH	170	11-OGly[(OAc)$_3$6'-OTig], 11β	195
Δ^{11}	120	Peroxy	145	O(Val-2'OH)	171	11-Oxyl-(OAc)$_3$, 11α	196
O(α-OH-dihydrocou)	121	α-Peroxy	146	α-O(Val-2'OH)	172	11-Oxyl-(OAc)$_3$, 11β	197
α-O(α-OH-dihydrocou)	122	β-Peroxy	147	β-O(Val-2'OH)	173	11-OAra, 11α	198
β-O(α-OH-dihydrocou)	123	OTig	148	OGly(2'-OGly)	174	11-OAra, 11β	199
OMeAcr-(4'OH)	124	α-OTig	149	α-OGly(2'-OGly)	175	11-NC, 11α	200
α-OMeAcr-(4'OH)	125	β-OTig	150	β-OGly(2'-OGly)	176	11-NC, 11 β	201

Appendix 1. (Continues): Substituents and their corresponding codes

Substituent	Code	Substituent	Code	Substituent	Code	Substituent	Code
Δ^{11}, 11α	202	14OH, 14α	206	11OCin, 11α	210	15-αOAc, 15α	214
Δ^{11}, 11β	203	14OH, 14 β	207	11OCin, 11β	211	15-αOAc, 15β	215
14-OGly, 14α	204	14Epoxy,14α	208	15-αOH, 15α	212		
14-OGly, 14β	205	14Epoxy, 14β	209	15-αOH, 15β	213		

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