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Demetallation of 1,3-diene products obtained from addition of natural products to tricarbonyl(cyclohexadienyl)iron tetrafluoroborate

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ABSTRACT

The demetallation of adducts obtained from the addition of biologically active natural products to [Fe (1-5-η-C_6H_7) $(CO)_3$][BF_4] using the oxidizing agent, trimethylamine-N-oxide, afford new organic compounds which are otherwise inaccessible by conventional organic techniques. The products of demetallation were characterized using NMR (^{1}H, ^{13}C), MS and IR spectroscopic measurements.

1. Introduction

The addition of organic substrates to coordinated π-hydrocarbon of the type [$M(CO)_3$(π-hydrocarbon)][BF_4] e.g [$Fe(CO)_3$(1-5-η-C_6H_7)][BF_4] (**I**) has led to the discovery of novel organometallic compounds such as 1,3-diene substituted products [1–6], 1,3,5-triene-sustituted products [7] or organometallic products [8]. We hereby report the addition of the biologically active natural products, gedunin, khivorin, polyavolensinol and 7-ketokhivorin to the complex [$Fe(CO)_3$(1-5-η-C_6H_7)][BF_4] to afford neutral substituted 1,3-diene products which on demetallation using the oxidizing agent, Me_3NO afforded novel organic compounds of potential medicinal value [9].

Gedunin is a tetranortriterpenoid and an active constituents of *Azadirachta indica A. Juss* and *Melia azedarach* (*L. Meliaceae*) [10], khivorin, and 7-ketokhivorin are isolates from *Khaya ivorensis* [11] and polyavolensinol, all exhibit medicinal characteristics and act as nucleophiles towards the dienylium cation (**I**) to form adducts. Polyavolensinol is obtained from the stem of *Polyathia suaveolens* [12], a medicinal tree grown in western part of Nigeria and used for treating blackwater fever and stomach disorder [13,14]. The adducts formed from the reaction of the dienylium cation (**I**) with the four natural products (Fig. 1) were spectroscopically characterized as well as the novel products obtained from the cleavage of the iron tricarbonyl moiety using Me_3NO.

2. Experimental

[Fe (1-5-η-C_6H_7) $(CO)_3$][BF_4] (**I**) complex was synthesized and purified using published procedure [15]. All the reagents used were obtained in their purest form available (BDH) and used without further purification. The natural products gedunin [10], khivorin [11] were pure, colourless crystalline solids and were isolated as reported in the literature. Polyavolensinol [12,13] is a lilac fluffy solid and 7-ketokhivorin, a light yellow crystal [11]. Infra red spectra were run on a Perkin Elmer Spectrum BX FTIR, and ^{1}H NMR (400 MHz) and ^{13}CNMR (100 MHz) were run on a Bruker AV 400 Spectrometer while the mass spectral measurements were carried out on a Micromass platform II Spectrometer and rotary evaporator for concentration of synthesized compounds.

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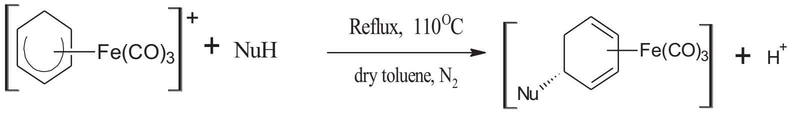
3. Equation for adduct formation



...........(1)

whereNuH=Gedunin/khivorin/7-ketokhivorin/polyavolensinol

where NuH = gedunin/khivorin/7-ketokhivorin/polyavolensinol

3.1. Products isolation and characterization

This was carried out using the method described by Odiaka et al. [16].

3.1.1. Tricarbonyl [1-4-η-5-(gedunino)cyclohexa-1,3-diene]iron (***II***)

(0.05 g, 0.1634 mmol) of [Fe (1-5-η-C_6H_7)(CO)$_3$][BF$_4$] and a two-fold molar excess of gedunin (0.157 g, 0.3268 mmol) was refluxed in a three-necked round-bottom flask (50 cm^3) under nitrogen in 30 ml dry toluene at 110 °C for 48 h. The mixture was allowed to cool to room temperature and then concentrated using rotary evaporator under reduced pressure to give a light yellow solid. This solid was shaken with (20/20, v/v) diethylether/water. The aqueous layer was set aside while the organic layer was concentrated using rotary evaporator under reduced pressure to give yellow oil. This was dried in a vacuum line for 3 h to give the same yellow oil (0.04 g, 35% yield). The IR √(CO) bands were observed at 2045 and 1970 cm^{-1}.

3.1.1.1. $C_{37}H_{40}O_{10}Fe$. Yellow oil, IR (film) $V_{\max}$ cm^{-1} = 2962 (C–H str of alkanes), 2045 & 1970 (√(CO) bands of coordinated diene of organometallic moiety), 1738 (C=O str of esters), 1667 (αβ-unsaturated ketone), 1495 (C–C band of C_6H_7), 1368 & 1163 (C–O str of esters), 874 (furan band) and 563 (Fe–C band). EMS *m*/*z* (relative intensity%): MS (700.7), 109 (8.125) [M − (2CO) − ($C_{32}H_{39}O_7$)], 150 (1.825) [M − (2CO) − ($C_{25}H_{26}O_7Fe$)], 201 (1.825) [M − (2CO)-($C_{25}H_{31}O_7$)], 257 (6.25) [M − (2CO) − ($C_{23}H_{29}O_5$) − (2H$^+$)], 401 (6.25) [M − (2CO) − ($C_{12}H_{10}O_2Fe$) − (H$^+$)], 500 (16.25) [M − (2CO) − ($C_3H_3O_3Fe$) − (H$^+$)], 505 (100) base peak [M − (2CO) − (C_5H_5OFe) − (2H$^+$)], 547 (8.125) [M − (2CO) − (C_2HOFe)], 546 (35) [M − (2CO) − (OHFe) − (H$^+$)], 604 (3.125) [M − (2CO) − (C_2HO)+(H$^+$)]. ^{1}H NMR (CDCl$_3$, 400 MHz δ ppm) see Table 1

3.1.2. Tricarbonyl[1,4-η-5-(khivorino)cyclohexa-1,3-diene]iron (***III***)

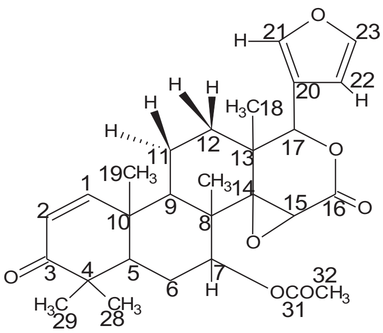
(0.025 g, 0.0817 mmol) of [Fe (1-5-η-C_6H_7)(CO)$_3$][BF$_4$] was weighed into the flask and a two-fold molar excess of khivorin (0.096 g, 0.1634 mmol) was added and refluxed in a three-necked round-bottom flask (50 cm^3) under nitrogen in 30 ml dry toluene at 110 °C for 48 h followed by similar work-up as for gedunin above. This gave yellow oil (0.024 g, 36% yield) which was dried on a vacuum line for 3 h. The IR √(CO) bands were observed at 2050 and 1980 cm^{-1}. The spectroscopic assignments for the products are reported below.

3.1.2.1. $C_{41}H_{48}O_{13}Fe$. Yellow oil, IR (film) $V_{\max}$ cm^{-1} = 2962 (C–H str of alkanes), 2050 & 1980 (√(CO) bands of coordinated diene of organometallic moiety), 1730 (C=O str ester), 1256, 1083 & 1013 (C–O str ester), 873 (furan band), 563 (Fe–C band). EMS *m*/*z* (relative intensity %): MS (804.8), 173 (2.27) [M − (2CO) − ($C_{31}H_{41}O_{10}$) − (2H$^+$)], 355 (1.135) [M − (2CO) − ($C_{22}H_{34}O_6$) + (H$^+$)], 541 (5)[M − (2CO) − ($C_9H_{10}O_2Fe$) − (H$^+$)], 609 (100) base peak [M-(2CO) − (C_5H_5OFe) − (2H$^+$)], 625 (2.27) [M − (2CO) − (C_4H_3OFe)], 687 (1.135) [M − (2CO) − ($C_2H_3O_2$) − (2H$^+$)]. ^{1}H NMR (CDCl$_3$, 400 MHz δ ppm): 4.55 (1H, m, H^1), 1.41 (2H, dd, H$^{2a\&2b}$), 4.45 (1H, m, H^3), 2.12 (1H, m, H^5), 2.16 (1H, m, H^{6b}), 4.64 (1H, m, H^7), 1.38 (1H, m, H^{11a}), 1.85 (1H, m, H^{11b}), 1.88 (1H, m, H^{12a}), 1.57 (1H, m, H^{12b}), 1.57 (1H, m, H^{12b}), 3.45 (1H, s, H^{15}), 1.17 (3H, s, H^{18}), 0.74 (3H, s, H^{19}), 6.24 (1H, s, H^{21}), 5.54 (1H, s, H^{22}), 0.85 (3H, s, H^{28}), 1.01 (3H, s, H^{29}), 0.94 (3H, s, H^{30}), 2.08 (3H, s, H^{32}), 1.95 (3H, s, H^{33}), 1.49 (3H, s, H^{34}), 7.33 (1H, d, H$^{3'}$), 2.79 (1H, m, H$^{2'}$), 1.60 (1H, m, H$^{6'a}$) and 2.19 (1H, m, H$^{6'b}$).

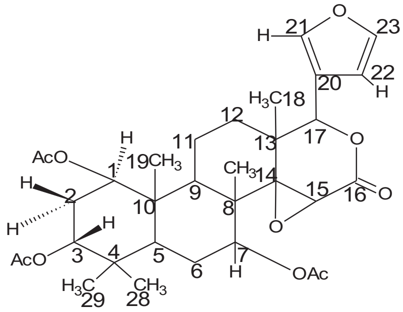
3.1.3. Tricarbonyl[1,4-η-5-(7-ketokhivorino)cyclohexa-1,3-diene] iron (***IV***)

(0.025 g, 0.0817 mmol) of [Fe (1-5-η-C_6H_7)(CO)$_3$][BF$_4$] was weighed into the flask followed by the addition of a two-fold excess of 7-ketokhivorin (0.0907 g, 0.1634 mmol). This was refluxed in 25 ml dry toluene for 48 h, followed by a similar work-up as for gedunin above which resulted into a yellow solid after drying on a vacuum line for 4 h. The yield, obtained was (0.028 g (44%)). The IR √(CO) band were observed at 2050 and 1980 cm^{-1}. Spectra data of the products are presented thus.

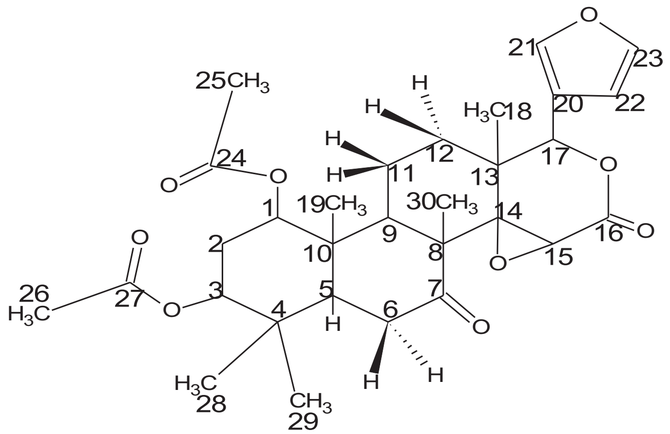
3.1.3.1. $C_{39}H_{44}O_{12}Fe$. Yellow solid, IR (film) $V_{\max}$ cm^{-1} = 2962 (C–H str of alkanes), 2050 & 1980 (√(CO) band of coordinated diene of organometallic moiety), 1728 (C=O str of ester), 1256, 1084 & 1012 (C–O str of ester), 873 (furan band), 565 (Fe–C band). EMS *m*/*z* (relative intensity%): MS (760.73), 191 (1.704) [M − (2CO) − ($C_{29}H_{37}O_8$)], 219 (2.840) [M − (2CO) − ($C_{27}H_{35} - O_8$) + (2H$^+$)], 541 (3.977) [M − (2CO) − (C_7H_7OFe)], 560 (1.704) [M − (2CO) − ($C_3H_3O_3Fe$)], 593 (3.977) [M − (2CO) − (C_3H_2OFe) − (H$^+$)], 609 (100) base peak [M − (2CO) − (C_2HOFe) + (2H$^+$)]. ^{1}H NMR (CDCl$_3$, 400 MHz, δ ppm): 4.65 (1H, t, H^1), 1.64 (1H, d, H^{2a}), 1.95 (1H, d, H^{2b}), 4.55 (1H, t, H^3), 2.12 (1H, t, H^5), 1.92 (1H, t, H^{6a}), 1.55 (1H, s, H^{6b}), 4.45 (1H, t, H^9), 1.50 (1H, s, H^{11a}), 1.88 (1H, t, H^{11b}), 2.16 (1H, d, H^{12a}), 1.57 (1H, t, H^{12b}), 3.45 (1H, s, H^{15}), 5.53 (1H, s, H^{17}), 0.94 (3H, s, H^{18}), 0.74 (3H, s, H^{19}), 7.17 (1H, s, H^{21}), 7.12 (1H, s, H^{22}), 2.08 (3H, s, H^{25}), 2.29 (3H, s, H^{26}), 1.01 (3H, s, H^{28}), 0.85 (3H,s, H^{29}), 7.33 (1H, m, H$^{1'}$), 7.34 (1H, t, H$^{2'}$), 6.24 (1H, dd, H$^{3'}$), 2.79 (1H, dd, H$^{5'}$), 1.60 (1H, d, H$^{6'a}$) and 2.19 (1H, d, H$^{6'b}$).



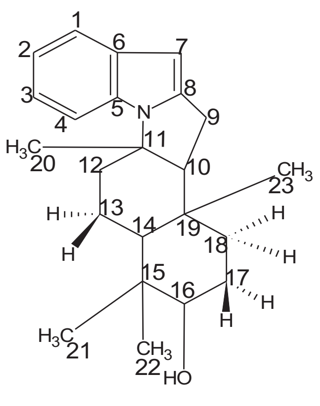
Gedunin



Khivorin



7-Ketokhivorin



Polyavolensinol

Fig. 1. Structures of natural products used.

Table 1
^{1}H NMR assignment of tricarbonyl [1-4-η-5-(gedunino) cyclohexa-1,3-diene]iron adduct.

Protons	Real spectra
H1	7.35(d)
H1′	5.82(s)
H11a	1.71(d)
H11b	1.77(t)
H12a	1.86(t)
H12b	2.04(s)
H15	3.46(s)
H17	5.55(s)
H18	1.18(s)
H19	1.16(s)
H2	5.79(s)
H2′	Pt of metallation
H21	7.30(s)
H22	7.02(s)
H28	1.09(s)
H29	1.50(s)
H3′	7.05(s)
H30	1.01(d)
H32	2.29(s)
H4′	6.27(t)
H5	1.74(t)
H5′	Not observed
H6a	1.66(d)
H6′a	Not observed
H6b	2.45(q)
H6′b	Not observed
H7	4.48(m)
H9	2.12(m)

Solvent signal = 7.19.

3.1.4. Tricarbonyl[1,4-η-5-(polyavolensinol)cyclohexa-1,3-diene] iron (***V***)

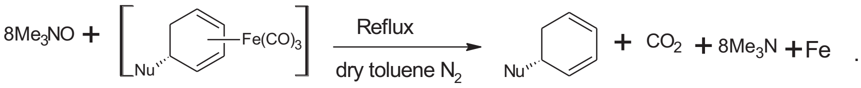
(0.025 g, 0.0817 mmol) of (1-5-η-C_6H_7)(CO)$_3$][BF$_4$] was weighed into the flask followed by the addition of two-fold molar excess of polyavolensinol (0.0551 g, 0.1634 mmol) and refluxing under nitrogen for 17 h. Similar work-up to that of gedunin above gave product (*V*) as a light lilac solid (0.024 g, 53% yield) after being concentrated and dried under vacuum for 3 h. The IR $\surd$(CO) bands were observed at 2045 and 1970 cm^{-1}. Spectroscopic data of the compound are:

3.1.4.1. $C_{32}H_{37}NO_4Fe$.

Light lilac solid, IR (film) $V_{\max}$ cm^{-1} = 2962 (C–H str of alkanes), 2042 & 1963 (($\surd$(CO)) bands of coordinated diene of organometallic moiety), 1453 (C–C str aromatic), 1258 (CH$_3$ of alkanes),1011 (C–O str alcohol), 853 (C–H out of plane), 580 & 561 (Fe–C band). EMS *m*/*z* (relative intensity %): MS (555.6), 207 (100) base peak [M − (2CO) − ($C_{16}H_{13}$ONFe) − (H$^+$)], 248 (29.375) [M − (2CO) − ($C_{16}H_{13}$ONFe) − (H$^+$)], 279 (8.750) [M − (2CO) − ($C_{15}H_{26}O$) + (2H$^+$)], 338 (7.500) [M − (2CO) − (C_7H_7OFe) + (2H$^+$)], 390 (8.750) [M − (2CO) − (C_3H_2OFe) + (H$^+$)], 467 (12.500) [M − (2CO) − (CH$_3$OH)], 485 (8.750) [M − (2CO) − (CH$_2$)]. ^{1}H NMR (CDCl$_3$, 400 MHz, δ ppm): 7.24 (1H, d, H^1), 7.46 (1H, t, H^2), 7.26 (1H, t, H^3), 7.47 (1H, d, H^4), 3.25 (1H, d, H^{9a}), 3.23 (1H, d, H^{9b}), 3.19 (1H, t, H^{10}), 2.63 (1H, d, H^{12a}), 1.98 (1H, t, H^{12b}), 1.54 (1H, t, H^{13a}), 2.29 (1H, s, H^{13b}), 2.56 (1H, t, H^{14}), 3.22 (1H, t, H^{16}), 2.60 (1H, d, H^{17a}), 1.49 (2H, s, H$^{17b\&20}$), 1.31 (1H, t, H^{18a}), 1.37 (1H, d, H^{18b}), 0.98 (3H, d, H^{21}), 1.14 (3H, s, H^{22}), 0.80 (3H, s, H^{23}), 6.10 (1H, s, OH proton), 6.97 (1H, d, H$^{1'}$), 7.00 (1H, d, H$^{3'}$), 6.93 (1H, t, H$^{4'}$), 2.73 (1H, q, H$^{5'}$) and 2.15 (1H, dd, H$^{6'b}$).

3.2. Demetallation of adducts

3.2.1. Demetallation reaction



.....(2)

where Nu = gedunin, khivorin, 7-ketokhivorin, polyavolensinol

*3.2.1.1. Tricarbonyl [1-4-η-5-(gedunino) cyclohexa-1,3-diene]iron (**VI**).* (0.1472 g, 0.2339 mmol) of the adduct was weighed into a three-necked round-bottom flask (50 cm^3) and an eight-fold molar excess of Me_3NO (0.1406 g, 1.8721 mmol) was added under nitrogen in 25 ml dry toluene. The solution was refluxed and the progress of the demetallation reaction was monitored by IR measurement on hourly basis until the disappearance of IR $\surd$(CO) bands at 2045 and 1970 cm^{-1} were observed. Demetallation reaction was completed in 3 h. The solution was allowed to cool to room temperature and was filtered under nitrogen through a celite column to give a yellow filtrate. This was concentrated on a rotary evaporator at reduced pressure to give yellow oil. The IR spectrum of the oil showed absence of the $\surd$(CO) bands earlier observed at 2045 and 1970 cm^{-1}. Depicted below are the spectroscopic parameters of the compound.

3.2.1.1.1. $C_{34}H_{40}O_7$. Yellow oil, IR (film) V_{max} cm^{-1} = 2962 (C—H str of alkanes), 1736 (C=O str ester), 1667 (αβ-unsaturated ketone), 1368 (C—H rock of alkanes), 1258 & 1232 (C—O str ester), 874 (furan band). EMS m/z (relative intensity%): MS (560.7), 151 (70.375) [M − $C_{24}H_{25}O_6$], 173 (100) base peak [M − $C_{23}H_{30}O_5$ − H^+],174 (6.25) [M − $C_{23}H_{30}O_5$], 422 (0.625) [M − $C_8H_{10}O_2$ − H^+], 500 (3.125) [M − $C_2H_3O_2$ − H^+]. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.35 (1H, d, H^1), 5.79 (1H, s, H^2), 1.77 (1H, d, H^{6a}), 2.43 (1H, q, H^{6b}), 4.49 (1H, m, H^7), 2.12 (1H, d, H^9), 1.74 (1H, t, H^{11a}), 1.86 (1H, t, H^{11b}), 1.89 (1H, m, H^{12a}), 1.80 (1H, t, H^{12b}), 3.46 (1H, s, H^{15}), 5.55 (1H, s, H^{17}), 1.56 (3H, s, H^{18}), 1.16 (3H, s, H^{19}), 7.05 (1H, s, H^{21}), 7.02 (1H, s, H^{22}), 1.09 (3H, s, H^{28}), 1.18 (3H, s, H^{29}), 1.01 (3H, d, H^{30}), 2.04 (3H, s, H^{32}), 5.81 (1H, s, $H^{1'}$), 6.27 (1H, t, $H^{4'}$), and 3.25 (1H, s, $H^{5'}$).

*3.2.1.2. Tricarbonyl[1-4-η-5-(khivorino)cyclohexa-1,3-diene]iron (**VII**).* (0.0994 g, 0.1235 mmol) of the adduct was weighed into the flask and an eight-fold molar excess of Me_3NO (0.0743 g, 0.9887 mmol) was added, followed by the addition of 25 ml dry toluene under nitrogen and refluxing at 110 °C. Similar work-up as for gedunin above gave yellow oil. Demetallation reaction was over in 3 h with the disappearance of the IR $\surd$(CO) bands at 2050 and 1980 cm^{-1}. Spectroscopic data for the products are:

3.2.1.2.1. $C_{38}H_{48}O_{10}$. Yellow oil, IR (film) V_{max} cm^{-1} = 2962 (C—H str of alkanes), 1728 (C=O str ester), 1257 & 1012 (C—O str ester),

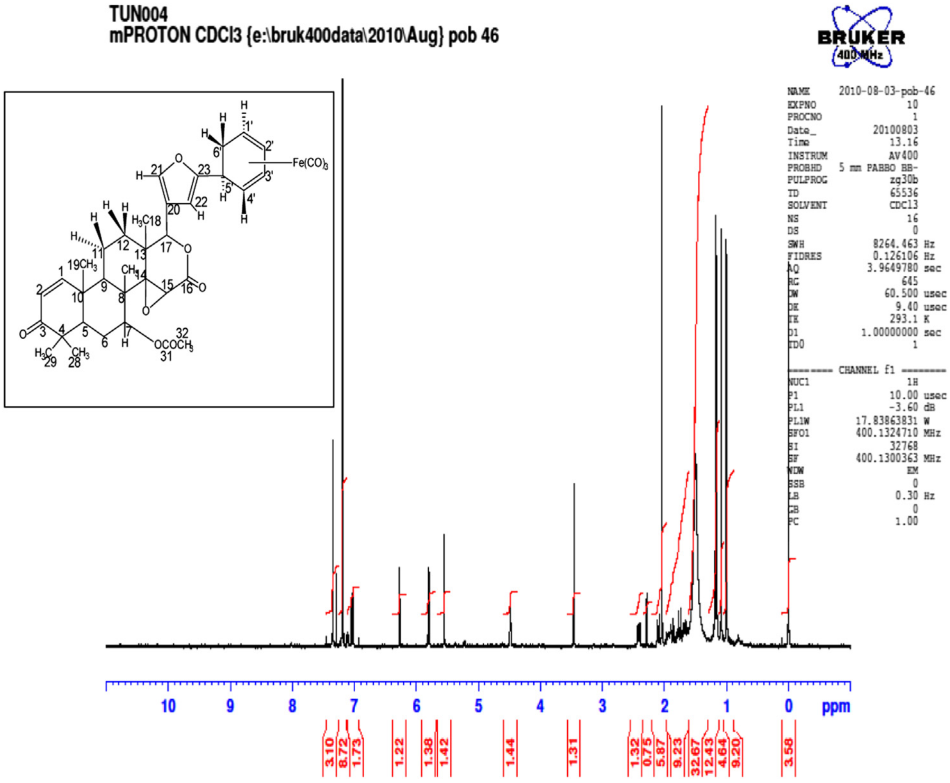
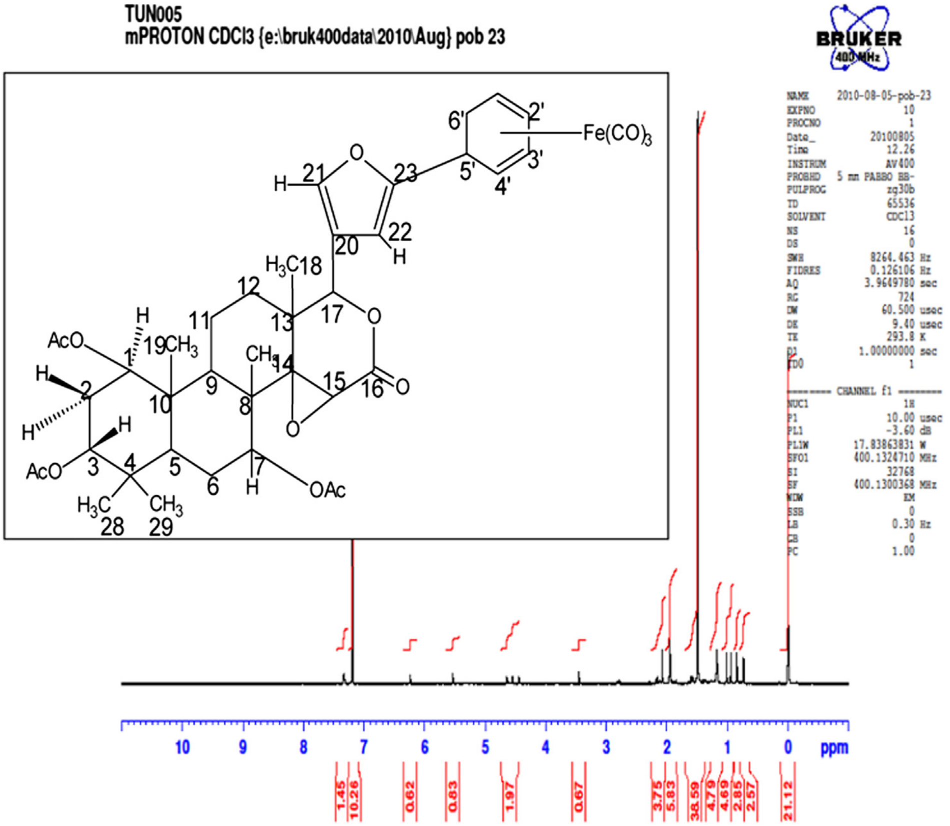


Fig. 2. ^{1}H NMR spectrum of tricarbonyl [1-4-η-5-(gedunino) cyclohexa-1,3-diene]iron.



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D1                1.00000000 sec
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LB                      0.30 Hz
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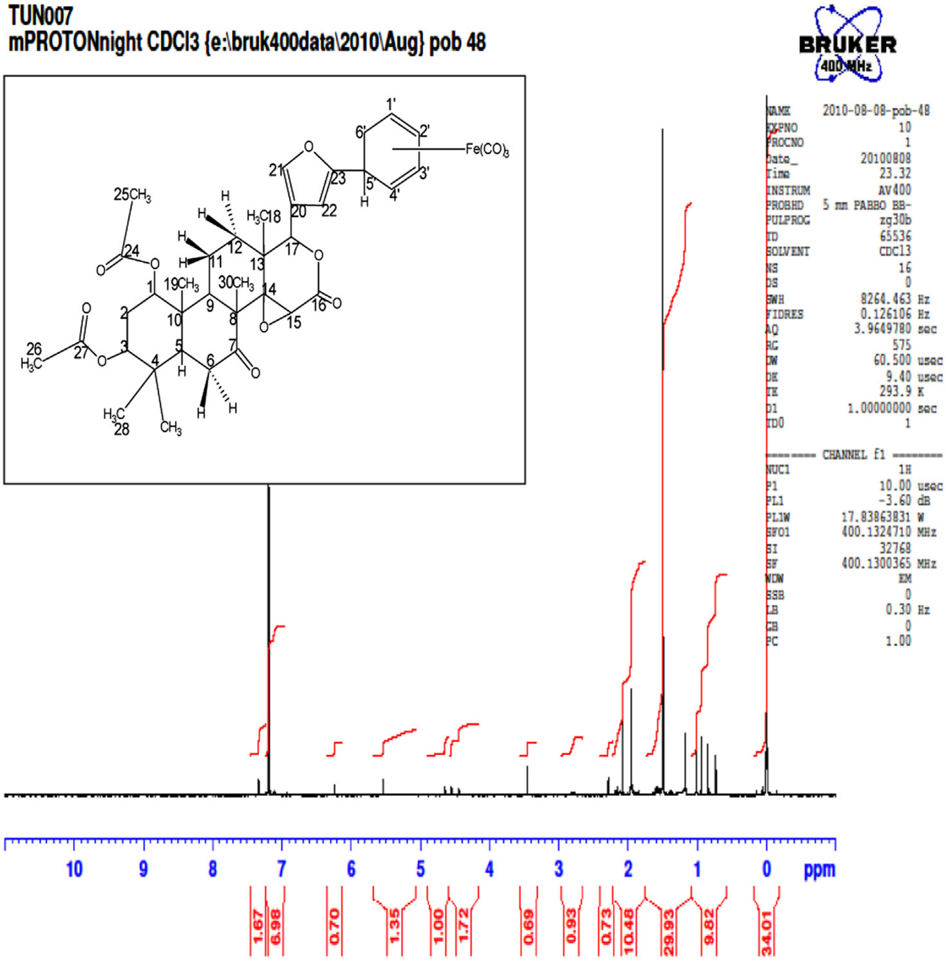
Fig. 3. ^{1}H NMR spectrum of tricarbonyl [1-4-η-5-(khivorino) cyclohexa-1,3-diene]iron.



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======== CHANNEL f1 ========
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Fig. 4. ^{1}H NMR spectrum of tricarbonyl [1-4-η-5-(7-keto-khivorino) cyclohexa-1,3-diene]iron.

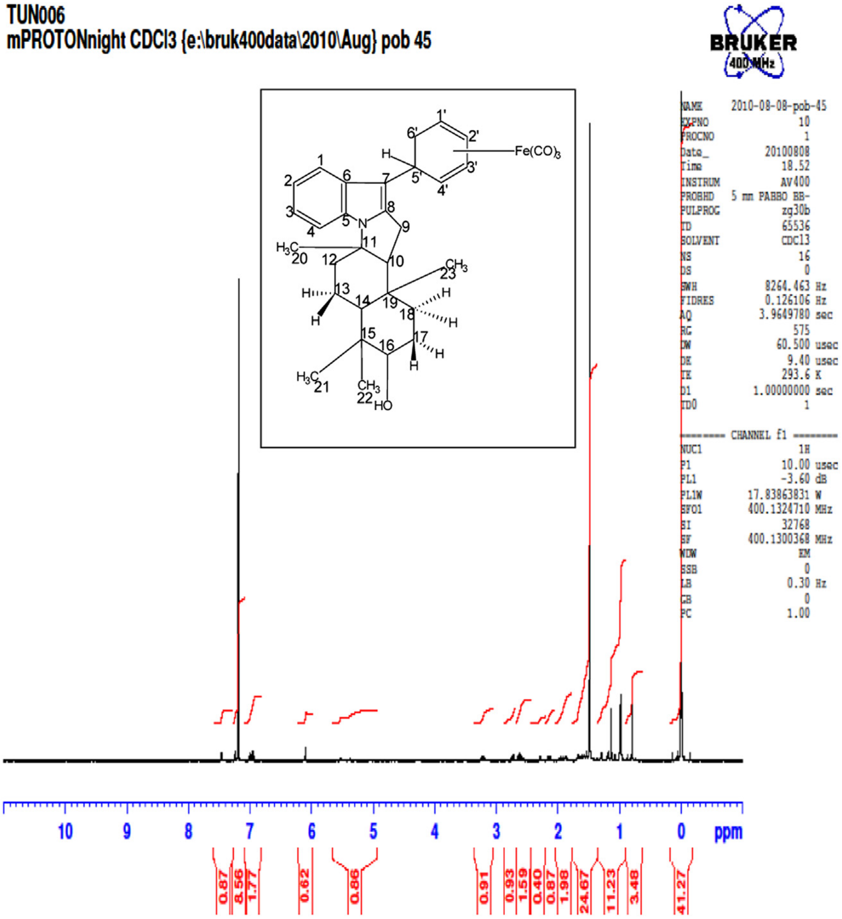


Fig. 5. ^{1}H NMR spectrum of tricarbonyl [1-4-η-5-(polyavolensinol) cyclohexa-1,3-diene]iron.

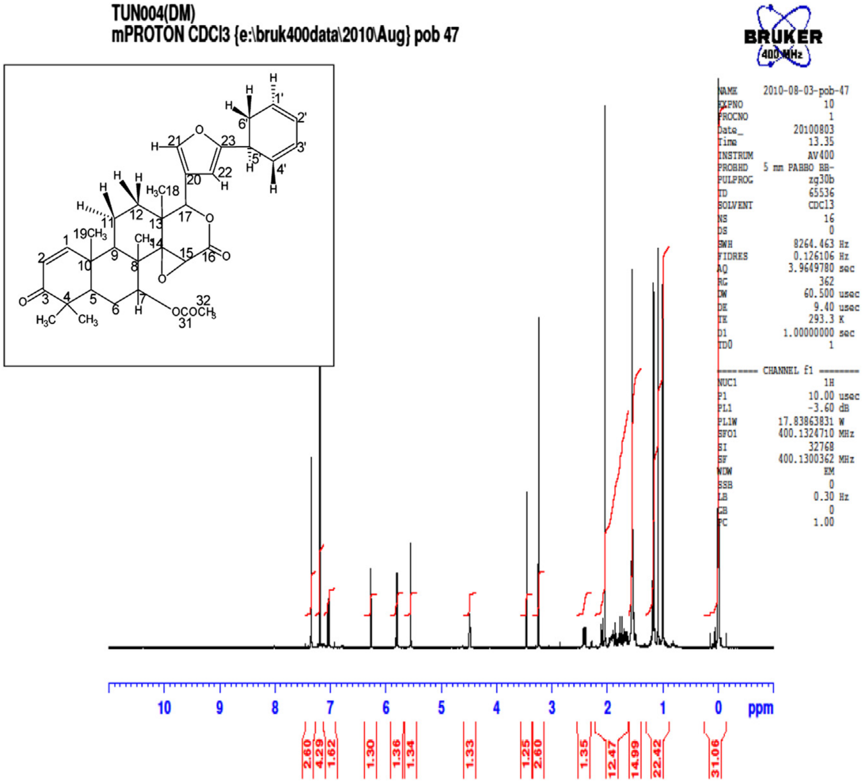


Fig. 6. ^{1}H NMR spectrum of 5-exo-(gedunino) cyclohexa-1,3-diene.

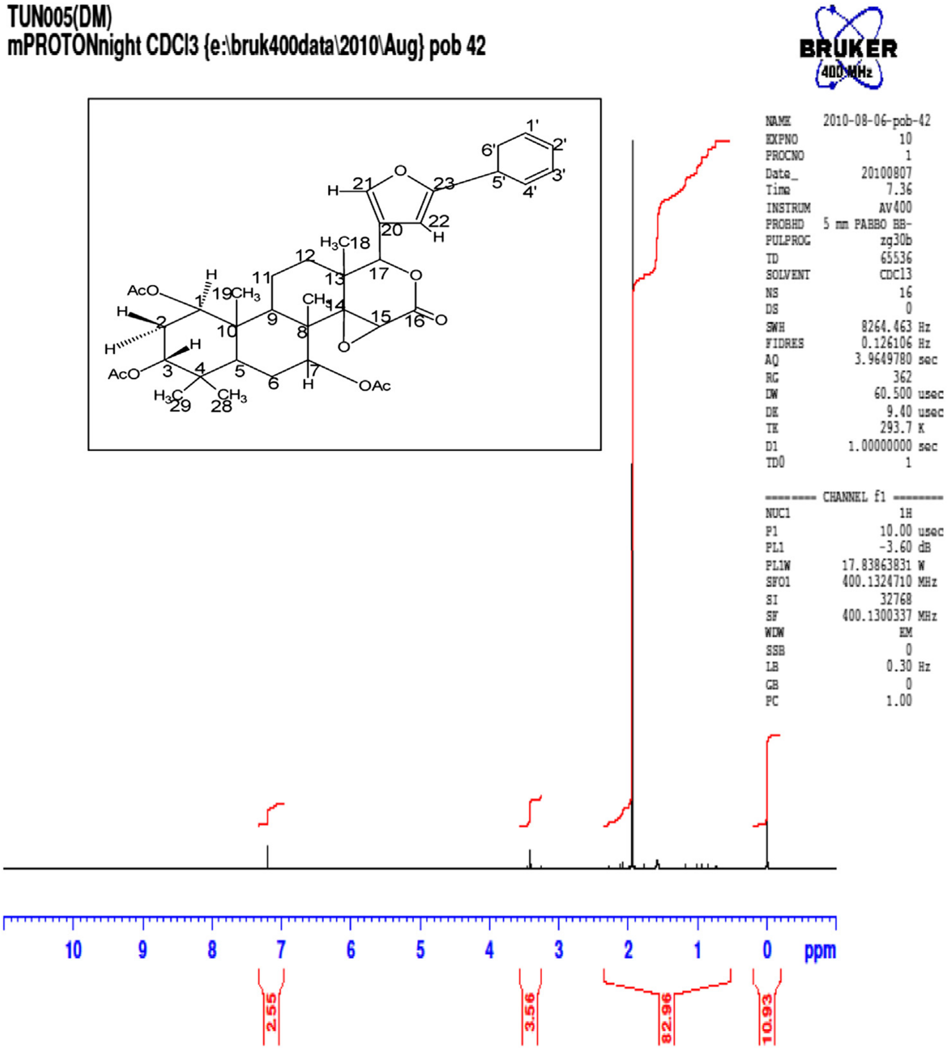


Fig. 7. ^{1}H NMR spectrum of 5-exo-(khivorino) cyclohexa-1,3-diene.

863 (furan band), 696 (C—H out of plane aromatics). EMS *m*/*z* (relative intensity%): MS (664.7), 173 (66.670) [M − $C_{27}H_{38}O_8$ − H^+], 271 (6.770) [M − $C_{22}H_{34}O_6$ + H^+], 560 (1.562) [M − C_8H_8], 609 (100) base peak [M − C_4H_5 − $2H^+$]. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 4.55 (1H, t, H^1), 1.90 (1H, s, H^{2a}), 1.95 (1H, s, H^{2b}), 4.45 (1H, t, H^3), 1.77 (1H, s, H^{6a}), 2.16 (1H, d, H^{6b}), 4.64 (1H, t, H^7), 1.58 (1H, s, H^{11a}), 2.04 (1H, d, H^{11b}), 2.00 (1H, d, H^{12b}), 3.45 (1H, s, H^{15}), 1.17 (3H, s, H^{18}), 0.74 (3H, s, H^{19}), 5.53 (1H, s, H^{22}), 0.85 (3H, s, H^{28}), 1.01 (3H, s, H^{29}), 0.94 (3H, s, H^{30}), 2.29 (3H, s, H^{32}), 2.11 (3H, s, H^{33}), 2.08 (3H, s, H^{34}), 7.33 (1H, m, $H^{1'}$), 6.24 (1H, dd, $H^{2'}$) and 7.35 (1H, t, $H^{3'}$).

*3.2.1.3. Tricarbonyl[1,4-η-5(7-ketokhivorino)cyclohexa-1,3-diene] iron (**VIII**).* (0.1562 g, 0.2017 mmol) of the adduct and an eight-fold molar excess of Me_3NO (0.1212 g, 1.61392 mmol) was added followed by the addition of 25 ml dry toluene under nitrogen and refluxing at 110 °C. Similar work-up as for gedunin above gave 5-exo-(7-ketokhivorino) cyclohexa-1,3-diene as yellow oil. Demetallation was over in 1 h, with the disappearance of the IR $\surd$(CO) bands at 2050 and 1980 cm^{-1}. The spectral data of the final product are:

3.2.1.3.1. $C_{36}H_{44}O_9$. Yellow oil, IR (film) V_{max} cm^{-1} = 2962 (C—H str of alkanes), 1728 (C=O str of ester), 1257 & 1014 (C—O str of ester), 874 (furan band). EMS *m*/*z* (relative intensity%): MS (620.7), 173 (3.409) [M − $C_{25}H_{34}O_7$ − H^+], 485 (2.840) [M − C_9H_9O − $2H^+$], 516 (0.586) [M − C_8H_8], 541 (2.840) [M − C_8H_8], 609 (100) base peak [M − CH + $2H^+$]. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 4.64 (1H, t, H^1), 1.95 (1H, d, H^{2a}), 4.55 (1H, t, H^3), 2.13 (1H, t, H^5), 1.92 (1H, t, H^{6a}), 1.57 (1H, d, H^{6b}), 4.45 (1H, t, H^9), 1.51 (1H, s, H^{11a}), 1.85 (1H, t, H^{11b}), 2.16 (1H, s, H^{12a}), 1.88 (1H, t, H^{12b}), 3.45 (1H, s, H^{15}), 5.53 (1H, s, H^{17}), 0.94 (3H, s, H^{18}), 0.73 (3H, s, H^{19}), 7.07 (1H, s, H^{21}), 2.08 (3H, s, H^{25}), 2.29 (3H, s, H^{26}), 1.01 (3H, s, H^{28}), 0.84 (3H, s, H^{29}), 7.33 (1H, m, $H^{1'}$), 7.34 (1H, t, $H^{2'}$), 6.24 (1H, dd, $H^{3'}$), 7.32 (1H, m, $H^{4'}$), 2.79 (1H, dd, $H^{5'}$), 1.63 (1H, d, $H^{6'a}$) and 2.19 (1H, d, $H^{6'b}$).

*3.2.1.4. Tricarbonyl[1,4-η-5(polyavolensinol)cyclohexa-1,3-diene]iron (**IX**).* (0.1358 g, 0.2446 mmol) of polyavolensinol adduct was weighed and an eight-fold molar excess of Me_3NO (0.1470 g, 1.9568 mmol) in 25 ml dry toluene under nitrogen and refluxed at 110 °C. Similar work-up as in gedunin above gave yellow oil which was sensitive to air. The demetallation was completed in 1.5 h. The spectral measurement are reported below:

3.2.1.4.1. $C_{29}H_{37}NO$. Yellow oil, IR (film) V_{max} cm^{-1} = 2961 (C—H str of alkanes), 1604 (C=C str aromatic), 1495 & 1453 (C—C str aromatic), 1258 & 1010 (C—O str alcohol), 790 (C—H out of plane).

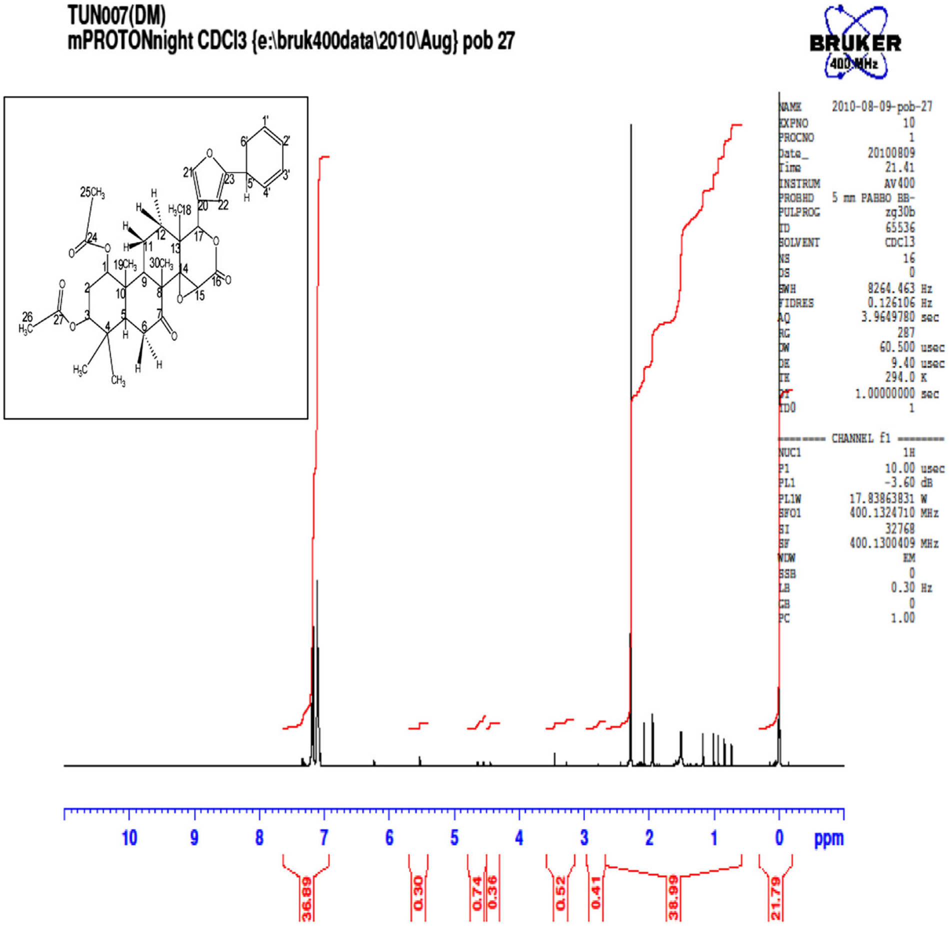
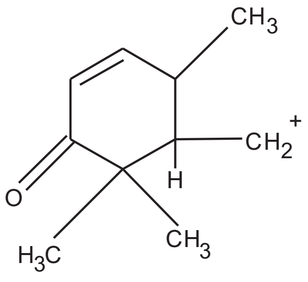


Fig. 8. ^1H NMR spectrum of 5-exo-(7-ketokhivorino) cyclohexa-1,3-diene.

4. Result and discussion

4.1. IR spectral studies of synthesised products

The reaction of [Fe (1-5-η-C_6H_7) $(CO)_3$][BF_4] (**I**) with gedunin, khivorin, 7-ketokhivorin and polyavolensinol in refluxing dry toluene affords the corresponding 1,3-diene substituted derivatives (**II**–**V**) above. These compounds and their demetallated derivatives are air sensitive yellow oils except for products (**IV**) and (**V**) which are respectively yellow and lilac solids. The adducts exhibited strong and intense IR $\surd$(CO) bands at ca 2050 and 1975 cm^{-1} characteristics of neutral tricarbonyl (1,3-diene-substituted)iron derivatives [1–6]. There is complete disappearance of IR $\surd$(CO) bands in all the demetallated products which confirms cleavage of the iron tricarbonyl moiety and hence complete demetallation is as presented in the experimental section.



151($C_{10}H_{15}O$)

Fig. 9. Mass fragment from adduct.

4.2. ^1H and ^{13}CNMR studies

The adducts and demetallated products are soluble in most organic solvents but 5-exo(polyavolensinol) cyclohexa-1,3-diene product (IX) is air-sensitive and insoluble in most solvents, thus preventing (^1H & ^{13}C)NMR and Mass spectral experiments. The ^1H NMR spectra of the tricarbonyl (5-exo-substituted) cyclohexa-1,3-diene products for Gedunin is presented in Table 1 while others are shown in the experimental section. The results clearly demonstrated coordination of the dienylium complex, [(1-5-η-C_6H_7)$Fe(CO)_3]^+$ (**I**) to the natural products to form the isolated 1,3-diene derivatives, (**II**–**V**). INDO molecule orbital calculations [17] on complex (**I**) show accumulation of positive charge on C^5 of the dienylium fragment and all the natural products (Fig. 1) attacked (**I**) at this point via the α-carbon of the furan ring for products (**II**), (**III**), and (**IV**) and via the β-carbon of the indole fragment for product (**V**). The ^1H NMR spectra of all the four products showed overlapping resonances characteristics of the outer ($H^{1,4}$) and inner ($H^{2,3}$) 1,3-diene protons at ca 7.33 and 5.14 ppm respectively while the $H^{5'}$ proton (bearing the C atom attached to the natural products) appears at ca 2.79 ppm.

The H^6 (exo) and $H^{6'}$ (endo) methylene protons of the coordinated diene resonate at ca 1.60 and 2.19 ppm respectively. These strong 1,3-diene resonance [1–6,18–21] clearly confirmed that

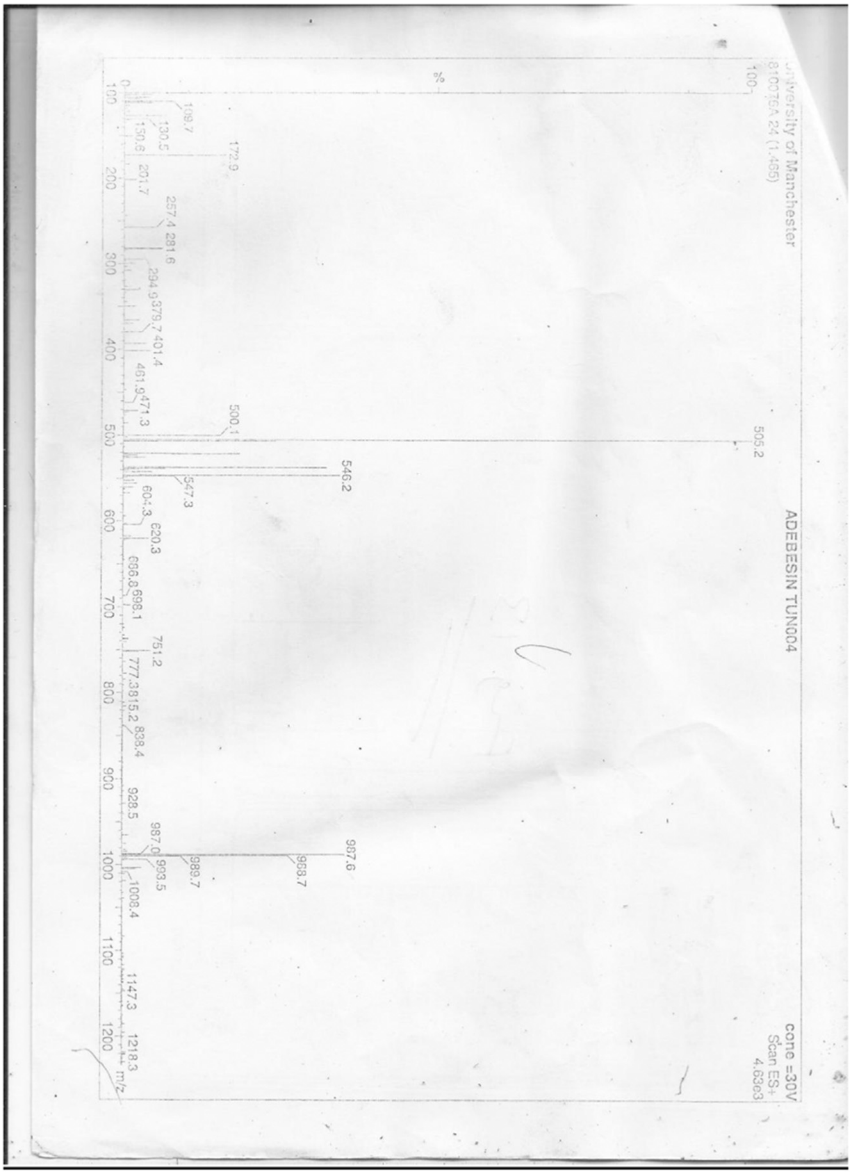


Fig. 10. Mass spectrum of tricarbonyl [1-4-η-5-(gedunino) cyclohexa-1,3-diene]iron.

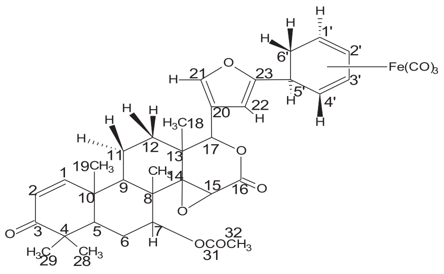
electrophilic attack by the dienylium cation (**I**) has occurred on the natural products to form the corresponding 1,3-diene-substituted products (**II**) to (**V**). In products (**II**), (**III**) and (**IV**) {see Figs. 2–4 respectively}, results confirmed the attachment of complex (**I**) to the α-carbon or C^{23} of the furan ring. For example, in (**II**), the doublet at 7.39 ppm which integrated for two protons (H^{21} and H^{23}) of the starting natural product, collapsed into singlet and integrated for only one proton (H^{21}) in the product (**II**) at a more shielded value of 7.30 ppm [Table 1 (Fig. 2)].

In addition, the complete disappearance of the proton resonance due to H^{23} in product (**II**) (Table 1) supported the addition of the organometallic complex (**I**) at C^{23} (or α-carbon of Gedunin). The ^1H NMR of the Khivorin and 7-ketokhivorin derivatives showed identical features to the Gedunin product. Our results are in agreement with the acetylation reactions of these natural products (Fig. 1) where electrophilic addition occurred at C^{23} of the furan ring [22]. However, in the gedunin reaction II, a mixture of acetylation products due to addition at C^{21} and C^{23} was observed [22]. Our observation of the addition of complex (**I**) on C^{23} of the furan ring in products (II) to (IV) must be attributed to steric hindrance due to approach of complex (**I**) at C^{21}. The ^1H NMR spectrum of tricarbonyl (1-4-η-5-exo(polyavolensinolino) cyclohexa1,3-diene) iron (**V**) is given in Fig. 5 while the proton assignments are given in the experimental section. In addition to the characteristics 1,3-diene proton resonances discussed earlier, one immediate observation is the complete disappearance of the proton resonance due to H^7, at the β-carbon of the indole fragment in the starting polyavolensinol located at 6.15 ppm. It is therefore obvious that complex (**I**) attacked the natural product at the β-carbon of the indole fragment to give product (**V**) as a stable lilac solid. The ^1H NMR spectra of the demetallated products are given in Fig. 6 (Gedunin), Fig. 7 (Khivorin) and Fig. 8 (7-ketokhivorin) respectively.

The ^{13}CNMR spectra were difficult to obtain due to the problem of low sample concentration.

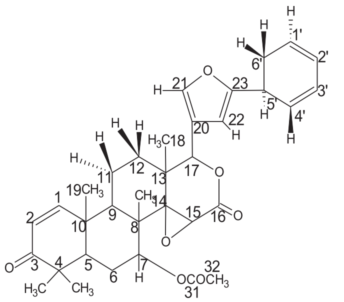
4.3. Mass spectra measurements

The mass spectral data for all the four compounds (**II**) to (**V**) are presented in the experimental section. All the products do not show the parent, $[P]^+$ ion expected at 700.7, 804.8, 760.7 and 555



Molecular Formula: $C_{37}H_{40}O_{10}Fe$ **Calculated mass = 700.677**

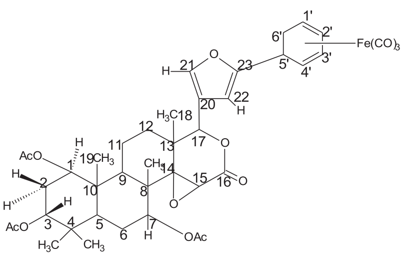
(a)Tricarbonyl [1-4-η-5-(gedunino) cyclohexa-1, 3-diene]iron



(b) 5-exo-(gedunino) cyclohexa-1,3-diene]iron

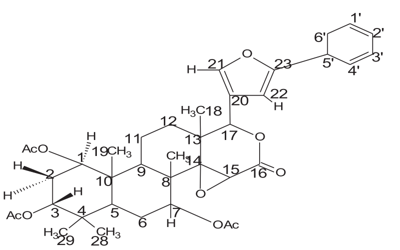
IUPACNAME:{1-[5(2,4-cyclohexadienyl)-3-furanyl]-1,3,3a,4b,5,6,6a,7,8,10a,10b,11,12,12a-tetradecahydro-4b,7,7,10a,pentamethyl-3,8-dioxooxireno[2,3-C]phenanthro[1,2-d]pyran-5-yl}ester acetic acid.

Molecular formula $C_{34}H_{40}O_7$ **Calculated mass = 560.677**



(c) Tricarbonyl [1-4-η-5-(khivorino) cyclohexa-1,3-diene]iron

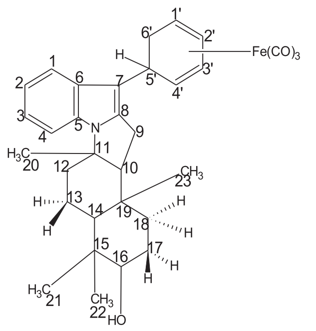
Molecular formula: $C_{41}H_{48}O_{13}Fe$ **Calculated mass = 804.782**



(d) 5-exo-(khivorino) cyclohexa-1,3-diene

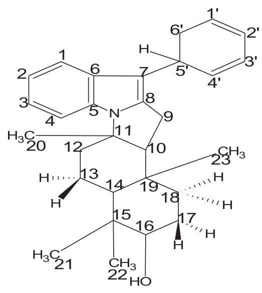
IUPACNAME:{5,10-bis(acethyoxy)-1-[5-(2,4-cyclohexadienyl)-3-furanyl]-1,3,3a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-hexadecahydro-4b,7,7,10a,12a-Pentamethyl-3-oxooxireno[2,3-C]phenanthro[1,2-d]pyran-8-yl) ester aceticacid.

Molecular formula $C_{38}H_{48}O_{10}$ **Calculated mass = 664.782**



(e) Tricarbonyl[1,4-η-5(polyavolensinolino)cyclohexa-1,3-diene]iron

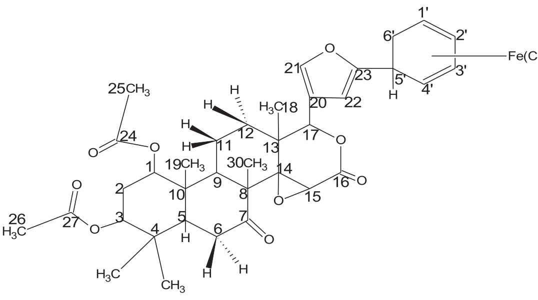
Molecular formula: $C_{32}H_{37}NO_4Fe$ **Calculated mass = 555**



(f) 5-exo-(polyavolensinolino)cyclohexa-1,3-diene

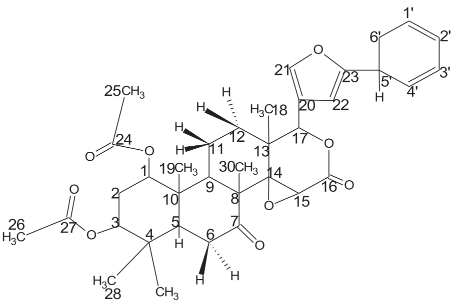
Molecular formula: $C_{29}H_{37}NO$ **Calculated mass = 415.61**

IUPAC NAME: 5-(2,4-cyclohexadienyl)-6a,7,7a,8,9,10,11,11a,12,12a-decahydro-7a,11,11,12a-Tetramethyl-6H-benzo[f]indolo[1,2-a)indol-10-ol



(g) Tricarbonyl[1,4-η-5(7-ketokhivorino)cyclohexa-1,3-diene]iron adduct

Molecular formula: $C_{39}H_{44}O_{12}Fe$ **Calculated mass = 760.73**

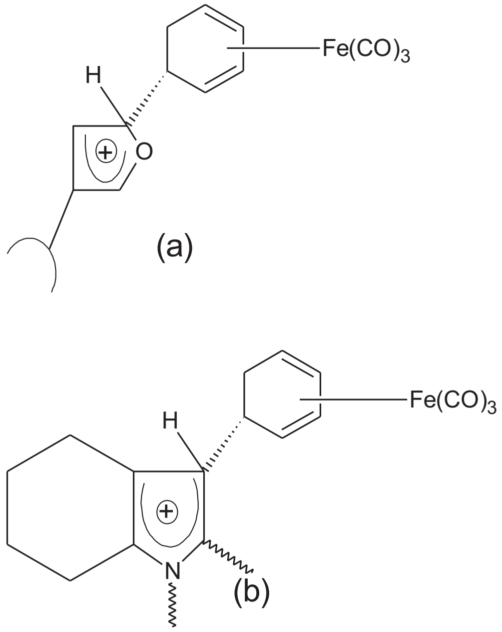


(h) 5-exo-(7-ketokhivorino)cyclohexa-1,3-diene

Molecular formula: $C_{36}H_{44}O_9$ **Calculated mass = 620.73**

IUPAC NAME: {10-(acethyloxy)-1-[5[2,4-cyclohexadienyl)-3-furanyl]-1,3,3a,4b,5,6,6a,7,8,9,10, 10a,10b,11,12,12a-hexadecahydro-4b,7,7,10a,12a-pentamethyl-3,5-dioxooxireno[2,3-c]phenanthro[1,2-d]pyran-8-yl}ester acetic acid.

Fig. 11. Structures of adducts and the demetallated products.



Scheme 1. Cationic intermediate complexes.

for product (**II**), (**III**), (**IV**), and (**V**) respectively. We observed the loss of α-β unsaturated ketone fragment in the gedunin adduct (Fig. 9) during the mass spectral measurement. The loss showed a strong peaks at 151 ($C_{10}H_{15}O$) (Fig. 10), thus explaining why our parent peaks, expected at 700.7 was not observed. We also observed the loss of (M-173) in all the compounds indicating weakness of the C (diene)–C (natural product) bond. Loss of the fragments from the adducts (**II**) to (**V**) in the mass spectral are not unusual as similar observations have been made [20,23,24] in the mass spectral studies of a wide range of tricarbonyl (1-4-η-5-exo-1,3-diene-substituted) iron complexes. We suggest that the adducts undergo thermal decomposition in the mass spectrometer, apparently due to the weakness of the C (diene)–C(natural products) bond.

The loss of a proton from each of the natural products to form the corresponding adducts (Equation (1)) is not unreasonable if one envisages the formation of cationic intermediate complexes of the type shown in the scheme for the furan and indole fragments of the products (**II**) to (**V**) (Fig. 11).

Thus, the well established electron-withdrawing character of the [(diene)Fe$(CO)_3$] moiety [25] allows rapid loss of hydrogen from the furan and indole (Scheme 1a & b) fragments at the point of coordination to give the isolated adducts.

Our demetallation studies represent the first of its kind in natural products organometallics. The complete absence of IR √(CO) bands in the 5-exo-(natural product) cyclohexa-1,3-diene derivatives confirmed the dislodgement of the Fe$(CO)_3$ unit in the parent adducts (**II**) to (**V**) to give the new organic derivatives.

We are currently carrying out detailed studies of the electrophilic attack of organometallics of the type [1-5-η-(dienyl)Fe $(CO)_3$] BF_4 (Dienyl=C_6H_7,2-MeOC_6H_6 or C_7H_9) on a wide range of natural products particularly from Nigerian trees. The resulting products and their demetallated analogues are been synthesized for the first time. These compounds are also been investigated for antimicrobial and antimycotic activities and our results will be the subject of subsequent publications.

Acknowledgements

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