Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

A polymorphic form of 4,4-Dimethyl-8-methylene-3-azabicyclo(3.3.1)non-2-en-2-yl 3-indolyl ketone, an indole alkaloid extracted from Aristotelia Chilensis (Maqui).

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Category: *communications (organic compounds)*

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A polymorphic form of 4,4-Dimethyl-8-methylene-3-azabicyclo(3.3.1)non-2-en-2-yl 3-indolyl ketone, an indole alkaloid extracted from *Aristotelia Chilensis* (Maqui).

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Abstract

The title compound (**II**) was obtained from mother liquors extracted from *Aristotelia Chilensis* (Commonly known as Maqui), a native chilean tree. The compound is a polymorphic form of the one obtained from the same source and reported in Watson, Nagl, Silva, Cespedes & Jakupovic (1989). *Acta Cryst.* C**45**, 1322–1324 (**Ia**).The molecule consists of an indole fragment and a nested three-ring system, both groups linked by a C-(CO)—C bridge. Comparison of both forms show that they do not differ in their gross features but in a couple of torsion angles in the central bridge. The resulting slight conformational differences reflect in a number of intramolecular contacts in **II** but unobserved in **Ia**. Regarding intermolecular interactions, both forms share a similar N—H···O synthon, but with diverse H-bonding strength, leading in both cases to C(6) catemers with different chain motives. There are some subtle differences between both forms regarding colour and the (de)location of a double bond, which allows to speculate about the possible existence of different variants of these type of molecules.

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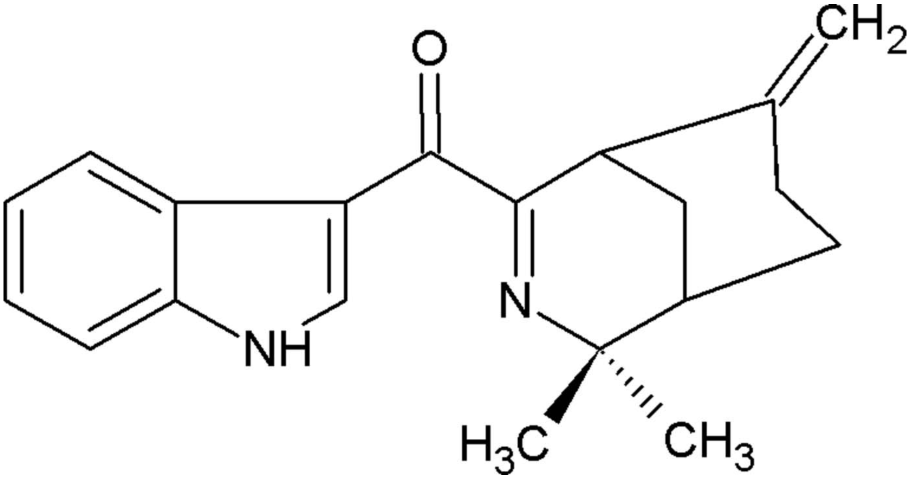

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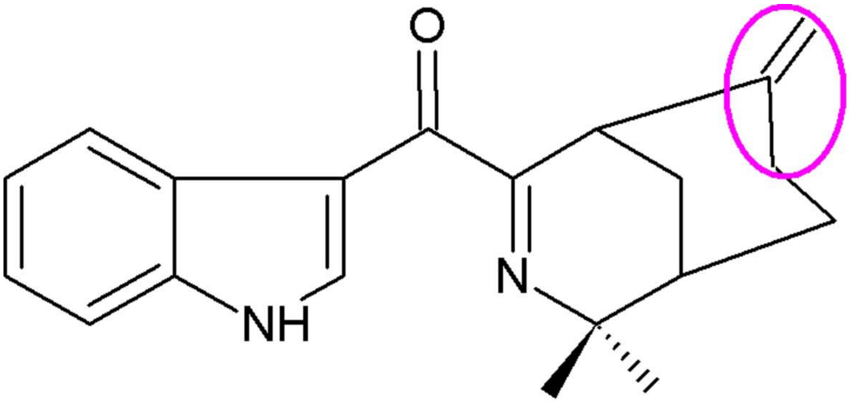

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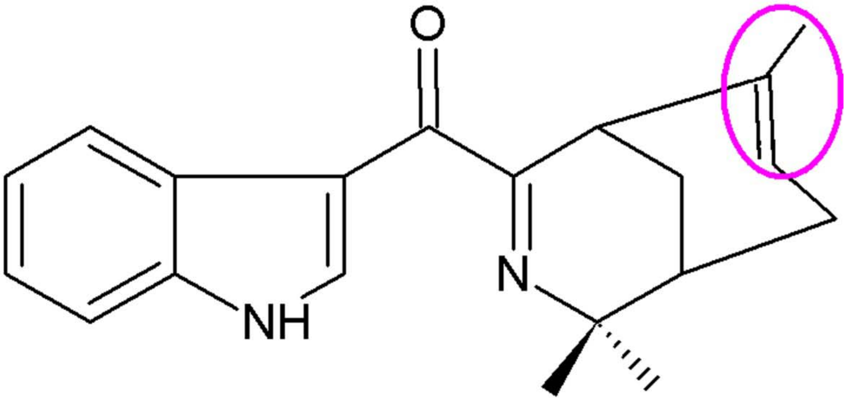

Ib

1. Introduction

Aristotelia Chilensis (Commonly known as Maqui) is a native chilean tree, which liquors show a variety of therapeutic properties known from ancient times by the original araucanian inhabitants. Studies during the ′70s and ′80s gave strong scientific support to this ancient knowledge: the tree has shown to produce an amazing quantity of molecular species of proved (or potential) pharmaceutical power; among others, a number of different indole alkaloids have been identified, some of them already known from other botanical species (*viz*., aristoteline, aristotelone (Bhakuni *et al.*, 1976), aristotelinine, aristone (Bittner *et al.*, 1978), and some other originally described from *Aristotelia Chilensis* extracts. One of this latter alkaloids was 4,4-Dimethyl-8-methylene-3-azabicyclo(3.3.1)non-2-en-2-yl 3-indolyl ketone, structurally characterized in Watson *et al.*, 1989, where two isomers of this molecule were mentioned as isolated from *Aristotelia Chilensis*. Both forms (Hereafter **Ia** and **Ib**) were characterized by NMR, and the results showed that the main difference resided in a double bond being either *exo* or *endo*-cyclic (Scheme2, encircled regions). The structure of only one of the two isomers was elucidated by single-crystal methods with an exocyclic double bond and an endocylic single one, and thus assigned to form **Ia**.

A recrystallization of a harvest of maqui liquors recently made in our laboratory provided a second crystallographic form of the same compound (hereafter **II**), and the crystal structural analysis herein reported primarily suggested the molecule to be a polymorph of **Ia** (Brief crystal data: both forms orthorhombic, $P2_12_12_1$, z=4, but: (**Ia**): ligh yellow crystals, a = 6.480 (1), b = 12.844 (2), c = 19.960 (3)Å); (**II**): deep red crystals, a = 9.7841 (5), b = 12.3479 (7); c = 13.8639 (5)Å)

We shall compare both structures in their gross features, as well as in the subtle differences telling both molecular forms apart.

2. Experimental

2.1. Isolation, purification and crystallization

Aristotelia chilensis (Maqui) was collected in Concepción, VIII Region of Chile (36°50′00" S and 73°01′54" O) in February 2012. 20 kg of leaves were dried at 40°C, powdered and macerated for 7 days in acid water with HCl pH 3, after that the water layer (50 L) was separated by filtration, basified with NaOH till pH 10 and extracted with EtOAc (3x20 L), the organic layer was concentrated in vacuo obtaining a crude alkaloid fraction. The alkaloid extract was chromatographed on aluminium oxide and eluted with hexane, hexane ethyl acetate 1:1, ethyl acetate, ethyl acetate methanol 8:2 gardient. The preparative chromatography was monitored by TLC (silica gel) and revealed with UV light and after Dragendorff's reagent; those fractions showing similar TLC patterns were pooled and subsequently purified by chromatography with the same procedure. From the hexane ethyl acetate 1:1 fraction deep red crystals were obtained ($[\alpha]_D^{25}$: +7.9 (c: 0.24, $CHCl_3$); mp= 256-257°C. ESI $[M+H]^+$: 307.1748.), which were further characterized by NMR (Table 4).

2.2. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1. All H atoms were found in a difference map, but C—H's were repositioned at their ideal values (*C—H*(methylene), 0.97 Å; C—H(aromatic), 0.93 Å; *C—H*(methyl), 0.96 Å. The only N-attached H was freely refined (N—H: 0.8 8(3)Å). In all cases, U_{iso}(H) was taken as U_{equiv}(Host). Due to the (expected) very small Bijvoet pair differences the absolute structure could not be reliably determined.

3. Results and discussion

Fig 1 shows an 30% probability level ellipsoid plot of **II**. Prima facie the unit does not substantially differ from **Ia** except in some torsion angles which determine their spatial stereochemistry, some of which are compared in Table 2. These torsion angles force in **II** a slightly more "open" conformation than for **Ia**, as shown in Fig 2, where an overlapp of both moieties is shown. A rough measure of this more open character can be found in the N1..N2 distances, 5.24 (2)Å in **Ia**, 5.63 (2)Å in **II**. This conformation seems to favour the existence of clear, though weak, C—H···N, C—H···O intra-moleculat interactions (Table 3, structure **II**, three upper entries, and Fig 1). Similar interactions are almost absent in **Ia**, were the only significant intramolecular contact (Table 3, structures **Ia**, first entry) is much weaker than its counterpart in **II**.

Regarding intermolecular interactions, both compounds share the same N—H···O synthon leading in both cases to C(6) catemers. There are, however, disimilar characteristics both in H-bond strength (Table 3, structure **II**, 4th entry, and structure **Ia**, 2nd entry) as in the resulting chain geometry (Fig 3): while the weak interaction in **Ia** leads to a translationally repetitive A—A—A motive along [100] (Fig 3a) the much stronger one in **II**, threaded along a two fold screw axis, leads to an alternating A—B—A—B motive along [001] (Fig 3b). Contrasting with what could be primarily expected from a mere analysis of H-bonding strengths, the chain in **Ia** is "shorter" ($a_{(\mathbf{Ia})} < 1/2\ c_{(\mathbf{II})}$ by nearly 7%). The ultimate reason is apparent from comparison of both chains in Figs 3a,3b: the very weakness of the N—H···O bond allows for a more closed <N—H—O> angle in **Ia**, thus letting molecules to approach each other. On the other hand, the more "straight" interaction in **II** sets molecules appart, with the result of a longer [001] chain.

The remaining interactions holding chain motives together are sensibly weaker, and unexceptional; they seem to be, however, more effective in **II**, since the original "shrinkage" in chain length in **Ia** (~7%) reduces to a mere 0.008% in cell volumes, the final result being a slightly more compact structure for this latter form (calculated densities: **Ia** 1.225gÅ^{-3}, **II** 1.215gÅ^{-3}).

Finally we shall analyze some subtleties differentiating **Ia** and **II** at a molecular level. A rather puzzling one is their striking colour difference (Ia, light yellowish; II, deep red) regardless of structural similarities. In this respect, the situation resembles much what reported in Yu, 2002. In this paper the difference in crystal colour, or "color polymorphism", was attributed to conformational differences between polymorphs, which would cause varying degrees of conjugation between aromatic chromophores. The commanding parameter would be in this case the torsion angle between aromatic rings, which with a drift from 104.7 (2)° to 52.6 (4)° to 21.7 (3)° (when going from one polymorph to another) could be responsible of a striking yellow-to-orange-to-red shift. In the Ia—II system there is in an anlogous situation, the equivalent groups being in this case the aromatic indole system and the planar portion of the heterocyclic six-membered ring, with dihedral angles of 47.2 (2)Å (in the yellowish Ia) and 21.3 (2)Å (in the deep red II). The striking similarity in colour shift, with an even tighter torsion angle span is apparent.

A perhaps related issue concerns the delocation of the terminal C—CH$_3$ <-> C═CH$_2$ bond. As previously stated, in Watson *et al.*, 1989 the authors differentiate the isomeric forms **Ia** and **Ib** by NMR results, ascribing **Ia** a double bond at C5═C20 (1.344 (8)Å, and a single one at C5—C16 (1.419 (9)Å). Unfortunately, no crystal data for **Ib** were available to confirm this difference by crystallographic means. When comparing these results with the present ones in **II**, the equivalent values herein found, C5═C20 (1.327 (7)Å) and C5—C16 (1.496 (7)Å) present a much clearer "double" and "single" character than those reported for **Ia**. In this sense, it is the present structure **II** which sems to be the one to be described as a pure, non-resonant moiety, while in **Ia** some delocalization between both *exo* and *endo* bonds seems to take place. In this context it is tempting to speculate about the possible existence of a continuous of resonant forms of the molecule, spontaneously occurring in the natural synthesis of the alkaloid. Unfortunatelly there is no satisfactory way to prove this kind of asserts regarding naturally occurring products, short of obtaining them by chance as in the present report.

fig1.tif

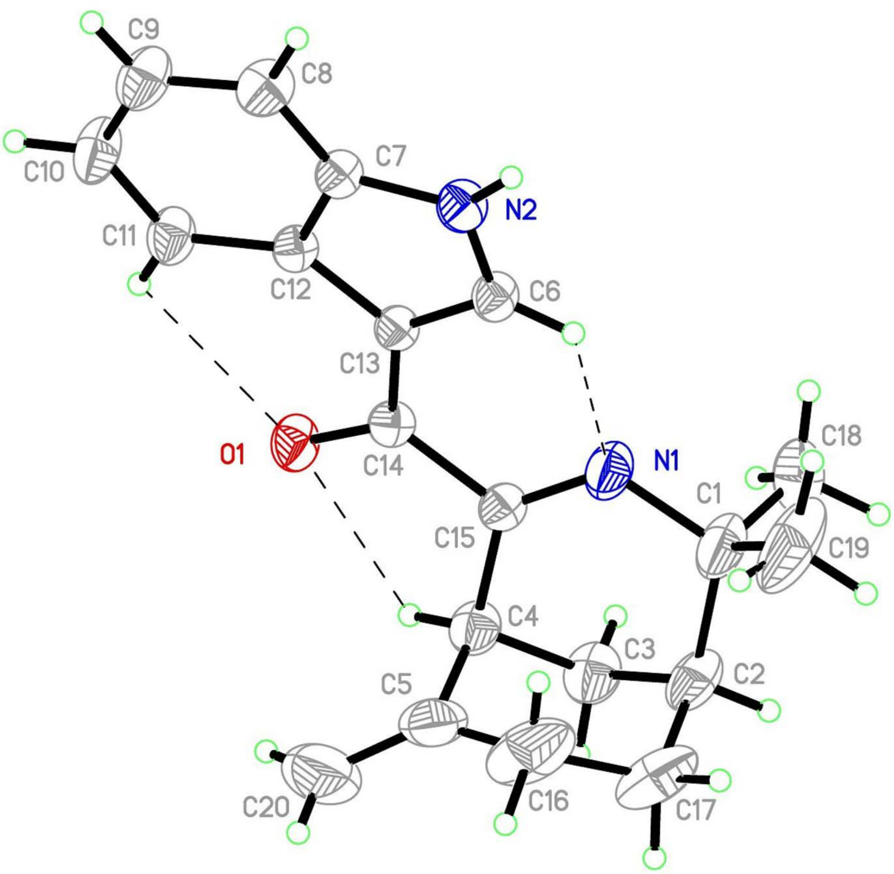

Figure 1

Ellipsoid plot of **II**, drawn at a 30% probability level. In broken lines, some relevant intramolecular H-bonding interactions.

fig2.tif

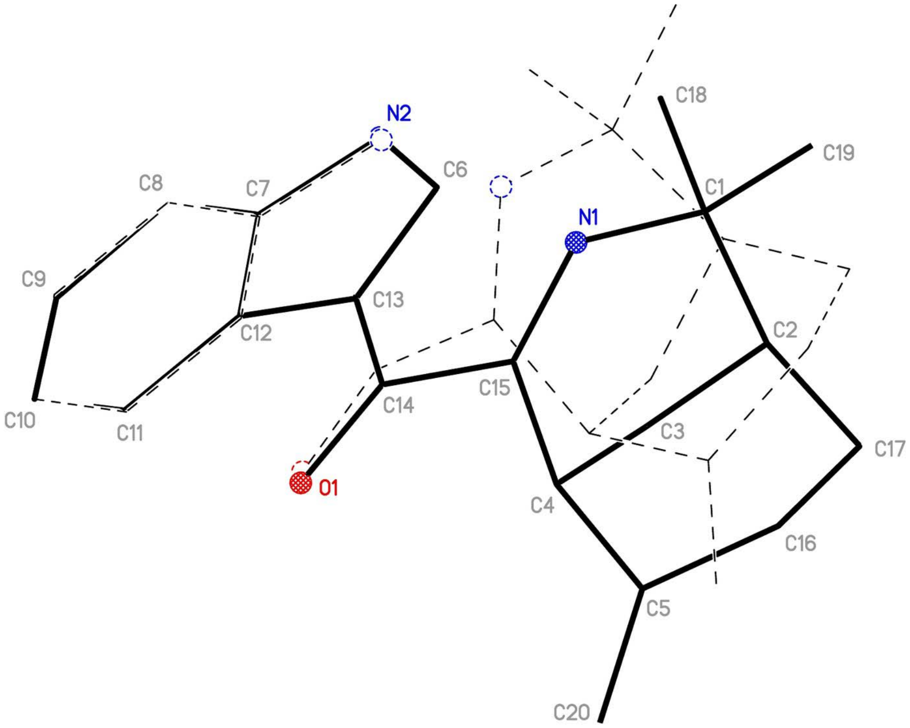

Figure 2

Comparison of the stereodisposition of the present structure **II**, in full lines and the one for **Ia**, in broken lines, after matching the almost identical indole groups.

fig3.tif

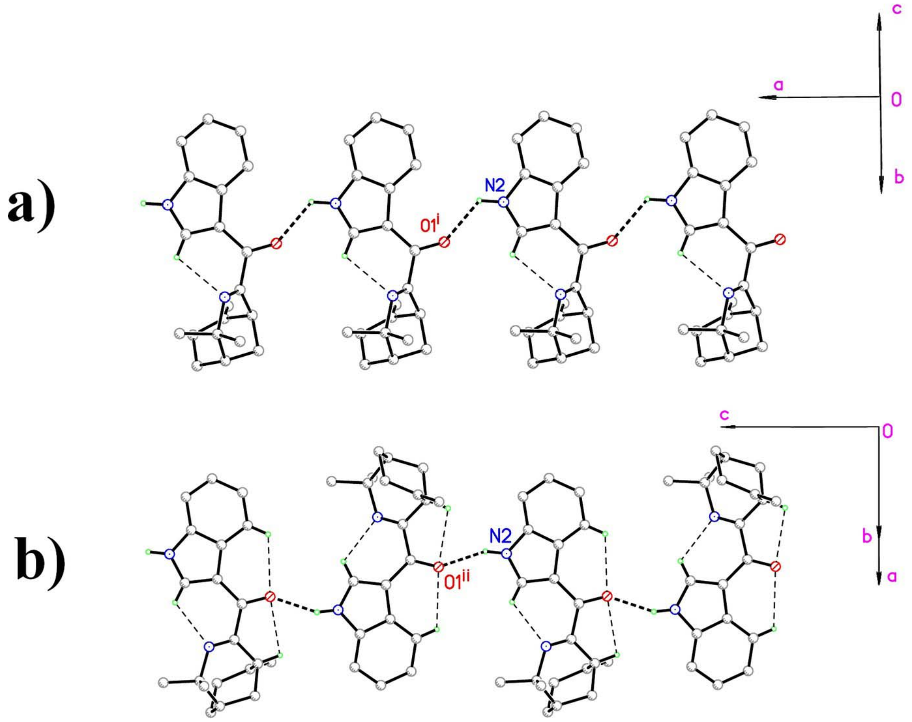

Figure 3

The chain structure in both compounds. a) Structure **Ia**, Symmetry code: (i) $x + 1, y, z$. b) Structure **II**, Symmetry code: (ii) $3/2 - x, -y, -1/2 + z$.

Table 1

Experimental details

Crystal data	
Chemical formula	$C_{20}H_{22}N_2O$
M_r	306.40
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	295
a, b, c (Å)	9.7841 (5), 12.3479 (7), 13.8639 (5)
V (Å^3)	1674.95 (14)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.08
Crystal size (mm)	0.32 × 0.18 × 0.10
Data collection	
Diffractometer	Oxford Diffraction Gemini CCD S Ultra diffractometer
Absorption correction	Multi-scan *CrysAlis PRO*, Oxford Diffraction (2009)
T_{min}, T_{max}	0.98, 0.99
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	4670, 3411, 2453
R_{int}	0.021

$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.679
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.054, 0.140, 1.02
No. of reflections	3411
No. of parameters	214
No. of restraints	0
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.15, −0.16

Computer programs: *CrysAlis PRO* (Oxford Diffraction, 2009), *CrysAlis PRO*, *SHELXS97* (Sheldrick, 2008), *SHELXL97* (Sheldrick, 2008), *SHELXTL* (Sheldrick, 2008), *SHELXL97*, *PLATON* (Spek, 2003).

Table 2

Comparison of Selected Torsion Angles (°)

Torsion Angle	**Ia**	**II**
C6—C13—C14—C15	-3.6 (7)	0.2 (4)
C13—C14—C15—N1	-47.8 (6)	-20.2 (3)

Table 3

Comparison of hydrogen-bond geometries for **II** and **Ia** (Å, °)

Symmetry codes: (i) 3/2-x,-y,-1/2+z, (ii) x+1, y, z.

Structure	D—H···A	D—H	H···A	D···A	D—H···A
II	C6—H6···N1	0.93	2.31	2.851 (4)	116
	C4—H4···O1	0.98	2.44	2.803 (3)	109
	C11—H11···O1	0.93	2.59	3.086 (3)	114
	N2—H2N···O1^{i}	0.88 (3)	2.03 (3)	2.852 (2)	154 (3)
Ia	C6—H6···N1	0.93	2.52	2.966 (6)	109
	N2—H2N···O1^{ii}	0.88	2.50	2.968 (6)	112

Table 4

Spectroscopic characterization of II by ^{1}H-NMR (CD_3OD, 600 MHz) and ^{13}C-NMR (CD_3OD, 150 MHz). (For site-codes see Fig.1)

Site	H (ppm)	C (ppm)	Site	H (ppm)	C (ppm)
1	-	60.3	11	8.28, m	123.0
2	1.90, t, 1.89	37.2	12	-	127.5
3	2.22, m 2.08, m	29.9	13	-	115.4
4	3.76, s	42.5	14	-	190.3
5	-	147.2	15	-	169.2
6	8.07, s	138.3	16	1.64, m 2.08, m	29.5
7	-	138.4	17	1.77, m 2.20, m	30.2
8	7.46, m	112.8	18	1.52	27.3
9	7.26, m	124.6	19	1.32	31.3
10	7.25, m	123.6	20	4.75, d, 1.7 4.70, d, 1.7	110.5

Acknowledgements

Authors would like to thank financial support given by project Fondecyt 3130378 and the University of Concepción. ANPCyT (PME 2006–01113), providing for for the purchase of the Oxford Gemini CCD diffractometer, is also acknowledged.

References

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Ellipsoid plot

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Hall group             P 2ac 2ab                 P 2ac 2ab
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Sum formula            C20 H22 N2 O              C20 H22 N2 O
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Dx,g cm-3              1.215                     1.215
Z                      4                         4
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F000'                  656.24
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PLAT242_ALERT_2_C Check Low       Ueq as Compared to Neighbors for         C5
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0 **ALERT level A** = Most likely a serious problem - resolve or explain

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0 ALERT level B = A potentially serious problem, consider carefully
8 ALERT level C = Check. Ensure it is not caused by an omission or oversight
3 ALERT level G = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
5 ALERT type 2 Indicator that the structure model may be wrong or deficient
3 ALERT type 3 Indicator that the structure quality may be low
3 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check
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reference checking results

The following references were not checked in detail as they were not recognized as journal references

Bhakuni, D. S., Silva, M., Matlin, S. A. & Sammes, P. G. (1976). Phytochemirtry, 15, 574-575.

Oxford Diffraction (2009). *CrysAlis PRO*, version 171.33.48. Oxford Diffraction Ltd, Abingdon, Oxfordshire, England.

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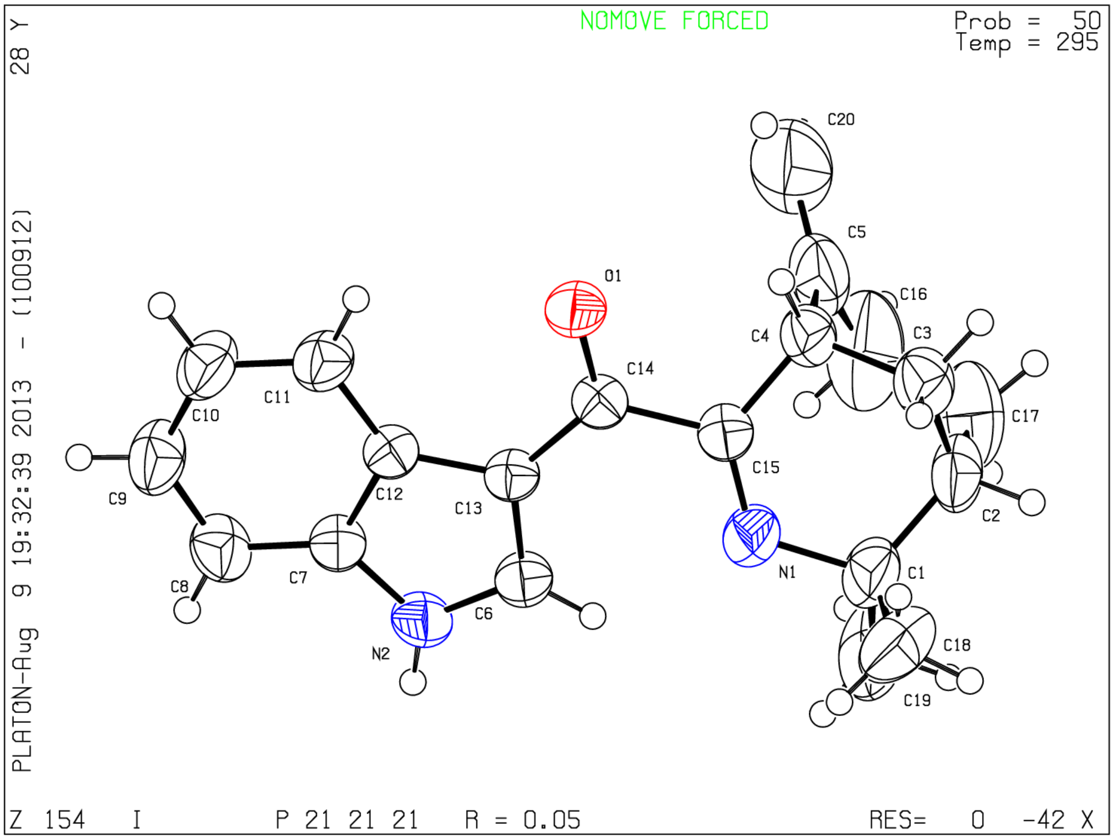
Bittner, M., Silva, M., Gopalakrishna, E. M., Watson, W. H., Zabel, V., Matlin, S. A. & Sammes, P. G. (1978). *J. Chem. Soc. Chem. Commun.* pp. 79--, 8O. is cited in the _related_literature **only**

Yu, L. (2002). *J. Phys. Chem. A*, **106**, 544--550. is cited in the _related_literature **only**

Datablock I - ellipsoid plot



supplementary materials

A polymorphic form of 4,4-Dimethyl-8-methylene-3-azabicyclo(3.3.1)non-2-en-2-yl 3-indolyl ketone, an indole alkaloid extracted from *Aristotelia Chilensis* (Maqui).

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Computing details

Data collection: *CrysAlis PRO* (Oxford Diffraction, 2009); cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXL97*, *PLATON* (Spek, 2003).

4,4-Dimethyl-8-methylene-3-azabicyclo(3.3.1)non-2-en-2-yl 3-indolyl ketone

Crystal data

$C_{20}H_{22}N_2O$
$M_r = 306.40$
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
$a = 9.7841$ (5) Å
$b = 12.3479$ (7) Å
$c = 13.8639$ (5) Å
$V = 1674.95$ (14) Å^3
$Z = 4$

$F(000) = 656$
$D_x = 1.215$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 1161 reflections
$\theta = 3.9$–$28.8°$
$\mu = 0.08$ mm^{-1}
$T = 295$ K
Prisms, red
0.32 × 0.18 × 0.10 mm

Data collection

Oxford Diffraction Gemini CCD S Ultra diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
ω scans, thick slices
Absorption correction: multi-scan *CrysAlis PRO*, Oxford Diffraction (2009)
$T_{min} = 0.98$, $T_{max} = 0.99$

4670 measured reflections
3411 independent reflections
2453 reflections with $I > 2\sigma(I)$
$R_{int} = 0.021$
$\theta_{max} = 28.9°$, $\theta_{min} = 3.9°$
$h = -13 \rightarrow 12$
$k = -8 \rightarrow 16$
$l = -10 \rightarrow 18$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.054$
$wR(F^2) = 0.140$
$S = 1.02$
3411 reflections
214 parameters
0 restraints
Primary atom site location: structure-invariant direct methods

Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0635P)^2 + 0.1599P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.15$ e Å^{-3}

$\Delta\rho_{\min} = -0.16$ e Å^{-3}

Extinction correction: *SHELXL*, $Fc^{*}=kFc[1+0.001xFc^{2}\lambda^{3}/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.014 (3)

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

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N1	0.5726 (3)	0.1765 (2)	0.85277 (16)	0.0653 (7)
N2	0.8665 (2)	−0.03048 (17)	0.73555 (14)	0.0515 (5)
H2N	0.881 (3)	−0.027 (2)	0.673 (2)	0.062*
C1	0.4690 (4)	0.2577 (3)	0.8245 (2)	0.0769 (10)
C2	0.3351 (3)	0.2516 (2)	0.8838 (2)	0.0683 (8)
H2	0.2903	0.3224	0.8791	0.082*
C3	0.3731 (4)	0.2346 (2)	0.98827 (19)	0.0684 (8)
H3A	0.2920	0.2374	1.0285	0.082*
H3B	0.4356	0.2908	1.0094	0.082*
C4	0.4408 (3)	0.1238 (2)	0.99661 (18)	0.0562 (7)
H4	0.4745	0.1136	1.0626	0.067*
C5	0.3393 (3)	0.0374 (3)	0.9736 (3)	0.0907 (11)
C6	0.7690 (3)	0.0262 (2)	0.78094 (14)	0.0465 (6)
H6	0.7132	0.0776	0.7517	0.056*
C7	0.9286 (3)	−0.10058 (19)	0.79999 (15)	0.0437 (6)
C8	1.0318 (3)	−0.1763 (2)	0.78454 (18)	0.0595 (7)
H8	1.0722	−0.1846	0.7243	0.071*
C9	1.0712 (3)	−0.2380 (2)	0.86195 (19)	0.0672 (8)
H9	1.1388	−0.2901	0.8538	0.081*
C10	1.0123 (3)	−0.2244 (2)	0.95220 (19)	0.0676 (8)
H10	1.0420	−0.2670	1.0034	0.081*
C11	0.9104 (3)	−0.1487 (2)	0.96750 (17)	0.0559 (7)
H11	0.8714	−0.1404	1.0282	0.067*
C12	0.8668 (2)	−0.08478 (18)	0.88987 (14)	0.0408 (5)
C13	0.7629 (2)	−0.00248 (18)	0.87737 (14)	0.0396 (5)
C14	0.6699 (2)	0.03597 (18)	0.95035 (15)	0.0412 (5)
C15	0.5589 (3)	0.11876 (19)	0.92747 (15)	0.0439 (6)
C16	0.2784 (4)	0.0504 (4)	0.8753 (4)	0.1232 (17)
H16A	0.2017	0.0011	0.8686	0.148*
H16B	0.3461	0.0311	0.8271	0.148*
C17	0.2296 (4)	0.1662 (4)	0.8570 (3)	0.1085 (14)
H17A	0.2069	0.1739	0.7892	0.130*
H17B	0.1470	0.1789	0.8939	0.130*
C18	0.5376 (5)	0.3683 (3)	0.8374 (3)	0.1200 (16)
H18A	0.5517	0.3819	0.9048	0.180*
H18B	0.4800	0.4237	0.8108	0.180*
H18C	0.6240	0.3686	0.8046	0.180*
C19	0.4439 (6)	0.2385 (5)	0.7166 (2)	0.142 (2)
H19A	0.5277	0.2486	0.6817	0.213*
H19B	0.3768	0.2890	0.6935	0.213*
H19C	0.4114	0.1660	0.7069	0.213*
C20	0.3082 (5)	−0.0406 (4)	1.0357 (5)	0.158 (2)

H20A	0.3502	−0.0425	1.0959	0.189*
H20B	0.2445	−0.0933	1.0191	0.189*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0665 (11)	0.0655 (11)	0.0329 (7)	0.0124 (10)	0.0034 (8)	0.0052 (8)
N1	0.0664 (15)	0.0780 (16)	0.0515 (12)	0.0245 (15)	0.0029 (11)	0.0160 (11)
N2	0.0576 (12)	0.0651 (13)	0.0317 (9)	0.0064 (12)	0.0043 (10)	0.0005 (9)
C1	0.082 (2)	0.091 (2)	0.0568 (16)	0.039 (2)	0.0002 (16)	0.0165 (15)
C2	0.0695 (18)	0.0718 (19)	0.0636 (16)	0.0343 (17)	−0.0032 (16)	−0.0085 (14)
C3	0.079 (2)	0.0678 (17)	0.0582 (16)	0.0216 (18)	0.0096 (15)	−0.0074 (13)
C4	0.0596 (16)	0.0590 (15)	0.0501 (13)	0.0141 (15)	0.0071 (13)	−0.0015 (12)
C5	0.0481 (16)	0.071 (2)	0.153 (4)	0.0041 (18)	0.017 (2)	0.006 (2)
C6	0.0503 (13)	0.0525 (14)	0.0367 (11)	0.0030 (13)	−0.0024 (10)	0.0006 (10)
C7	0.0468 (13)	0.0478 (13)	0.0365 (11)	0.0012 (12)	−0.0034 (11)	−0.0040 (10)
C8	0.0652 (17)	0.0686 (17)	0.0445 (13)	0.0119 (16)	0.0029 (12)	−0.0127 (12)
C9	0.077 (2)	0.0634 (17)	0.0609 (17)	0.0259 (18)	−0.0044 (15)	−0.0082 (13)
C10	0.086 (2)	0.0669 (17)	0.0500 (14)	0.0273 (18)	−0.0066 (15)	0.0064 (13)
C11	0.0674 (17)	0.0592 (15)	0.0412 (12)	0.0107 (14)	−0.0019 (13)	0.0023 (11)
C12	0.0438 (12)	0.0434 (12)	0.0352 (11)	−0.0011 (11)	−0.0037 (10)	−0.0026 (9)
C13	0.0415 (11)	0.0434 (12)	0.0339 (10)	−0.0020 (10)	−0.0040 (10)	−0.0007 (9)
C14	0.0429 (12)	0.0466 (12)	0.0343 (10)	−0.0017 (11)	−0.0034 (10)	−0.0038 (9)
C15	0.0454 (13)	0.0491 (13)	0.0373 (11)	0.0021 (12)	−0.0044 (10)	−0.0038 (10)
C16	0.070 (2)	0.097 (3)	0.204 (5)	−0.007 (2)	−0.049 (3)	−0.039 (3)
C17	0.062 (2)	0.129 (4)	0.135 (3)	0.026 (2)	−0.033 (2)	−0.025 (3)
C18	0.113 (3)	0.090 (3)	0.157 (4)	0.021 (3)	0.010 (3)	0.062 (3)
C19	0.166 (5)	0.213 (5)	0.0476 (18)	0.122 (4)	−0.002 (2)	0.018 (2)
C20	0.090 (3)	0.096 (3)	0.288 (7)	−0.005 (3)	0.055 (4)	0.052 (4)

Geometric parameters (Å, º)

O1—C14	1.238 (3)	C8—C9	1.372 (4)
N1—C15	1.265 (3)	C8—H8	0.9300
N1—C1	1.479 (4)	C9—C10	1.387 (4)
N2—C6	1.340 (3)	C9—H9	0.9300
N2—C7	1.384 (3)	C10—C11	1.384 (4)
N2—H2N	0.88 (3)	C10—H10	0.9300
C1—C18	1.532 (6)	C11—C12	1.401 (3)
C1—C19	1.534 (5)	C11—H11	0.9300
C1—C2	1.549 (4)	C12—C13	1.447 (3)
C2—C3	1.509 (4)	C13—C14	1.442 (3)
C2—C17	1.522 (5)	C14—C15	1.525 (3)
C2—H2	0.9800	C16—C17	1.529 (6)
C3—C4	1.525 (4)	C16—H16A	0.9700
C3—H3A	0.9700	C16—H16B	0.9700
C3—H3B	0.9700	C17—H17A	0.9700
C4—C5	1.492 (4)	C17—H17B	0.9700
C4—C15	1.503 (4)	C18—H18A	0.9600
C4—H4	0.9800	C18—H18B	0.9600

C5—C20	1.327 (5)	C18—H18C	0.9600
C5—C16	1.496 (5)	C19—H19A	0.9600
C6—C13	1.384 (3)	C19—H19B	0.9600
C6—H6	0.9300	C19—H19C	0.9600
C7—C8	1.392 (3)	C20—H20A	0.9300
C7—C12	1.399 (3)	C20—H20B	0.9300

C15—N1—C1	121.8 (3)	C11—C10—H10	119.4
C6—N2—C7	109.63 (19)	C9—C10—H10	119.4
C6—N2—H2N	123.4 (18)	C10—C11—C12	118.8 (2)
C7—N2—H2N	126.7 (18)	C10—C11—H11	120.6
N1—C1—C18	105.8 (3)	C12—C11—H11	120.6
N1—C1—C19	105.3 (3)	C7—C12—C11	118.3 (2)
C18—C1—C19	108.8 (4)	C7—C12—C13	107.15 (18)
N1—C1—C2	113.9 (2)	C11—C12—C13	134.5 (2)
C18—C1—C2	110.6 (3)	C6—C13—C14	128.4 (2)
C19—C1—C2	112.0 (3)	C6—C13—C12	105.38 (19)
C3—C2—C17	107.7 (3)	C14—C13—C12	126.19 (18)
C3—C2—C1	108.0 (3)	O1—C14—C13	120.8 (2)
C17—C2—C1	118.5 (3)	O1—C14—C15	117.59 (19)
C3—C2—H2	107.4	C13—C14—C15	121.64 (18)
C17—C2—H2	107.4	N1—C15—C4	125.5 (2)
C1—C2—H2	107.4	N1—C15—C14	118.2 (2)
C2—C3—C4	107.8 (2)	C4—C15—C14	116.26 (19)
C2—C3—H3A	110.2	C5—C16—C17	112.1 (3)
C4—C3—H3A	110.2	C5—C16—H16A	109.2
C2—C3—H3B	110.2	C17—C16—H16A	109.2
C4—C3—H3B	110.2	C5—C16—H16B	109.2
H3A—C3—H3B	108.5	C17—C16—H16B	109.2
C5—C4—C15	110.2 (2)	H16A—C16—H16B	107.9
C5—C4—C3	109.6 (3)	C2—C17—C16	113.3 (3)
C15—C4—C3	108.8 (2)	C2—C17—H17A	108.9
C5—C4—H4	109.4	C16—C17—H17A	108.9
C15—C4—H4	109.4	C2—C17—H17B	108.9
C3—C4—H4	109.4	C16—C17—H17B	108.9
C20—C5—C4	122.1 (4)	H17A—C17—H17B	107.7
C20—C5—C16	125.3 (4)	C1—C18—H18A	109.5
C4—C5—C16	112.5 (3)	C1—C18—H18B	109.5
N2—C6—C13	110.5 (2)	H18A—C18—H18B	109.5
N2—C6—H6	124.7	C1—C18—H18C	109.5
C13—C6—H6	124.7	H18A—C18—H18C	109.5
N2—C7—C8	129.7 (2)	H18B—C18—H18C	109.5
N2—C7—C12	107.3 (2)	C1—C19—H19A	109.5
C8—C7—C12	123.0 (2)	C1—C19—H19B	109.5
C9—C8—C7	117.2 (2)	H19A—C19—H19B	109.5
C9—C8—H8	121.4	C1—C19—H19C	109.5
C7—C8—H8	121.4	H19A—C19—H19C	109.5
C8—C9—C10	121.4 (3)	H19B—C19—H19C	109.5
C8—C9—H9	119.3	C5—C20—H20A	120.0

C10—C9—H9	119.3	C5—C20—H20B	120.0
C11—C10—C9	121.3 (2)	H20A—C20—H20B	120.0

C15—N1—C1—C18	112.2 (3)	C8—C7—C12—C13	−178.5 (2)
C15—N1—C1—C19	−132.6 (4)	C10—C11—C12—C7	0.0 (4)
C15—N1—C1—C2	−9.5 (4)	C10—C11—C12—C13	177.5 (3)
N1—C1—C2—C3	42.3 (4)	N2—C6—C13—C14	−177.6 (2)
C18—C1—C2—C3	−76.7 (3)	N2—C6—C13—C12	−0.4 (3)
C19—C1—C2—C3	161.7 (3)	C7—C12—C13—C6	−0.1 (2)
N1—C1—C2—C17	−80.4 (4)	C11—C12—C13—C6	−177.8 (3)
C18—C1—C2—C17	160.5 (3)	C7—C12—C13—C14	177.2 (2)
C19—C1—C2—C17	39.0 (4)	C11—C12—C13—C14	−0.5 (4)
C17—C2—C3—C4	63.7 (3)	C6—C13—C14—O1	178.3 (2)
C1—C2—C3—C4	−65.4 (3)	C12—C13—C14—O1	1.7 (3)
C2—C3—C4—C5	−65.5 (3)	C6—C13—C14—C15	0.2 (4)
C2—C3—C4—C15	55.1 (3)	C12—C13—C14—C15	−176.5 (2)
C15—C4—C5—C20	118.3 (4)	C1—N1—C15—C4	−0.4 (4)
C3—C4—C5—C20	−121.9 (4)	C1—N1—C15—C14	179.1 (2)
C15—C4—C5—C16	−62.3 (3)	C5—C4—C15—N1	97.4 (3)
C3—C4—C5—C16	57.5 (4)	C3—C4—C15—N1	−22.9 (4)
C7—N2—C6—C13	0.7 (3)	C5—C4—C15—C14	−82.2 (3)
C6—N2—C7—C8	178.2 (3)	C3—C4—C15—C14	157.5 (2)
C6—N2—C7—C12	−0.8 (3)	O1—C14—C15—N1	161.6 (2)
N2—C7—C8—C9	−177.9 (3)	C13—C14—C15—N1	−20.2 (3)
C12—C7—C8—C9	0.9 (4)	O1—C14—C15—C4	−18.8 (3)
C7—C8—C9—C10	−1.0 (5)	C13—C14—C15—C4	159.5 (2)
C8—C9—C10—C11	0.7 (5)	C20—C5—C16—C17	131.1 (4)
C9—C10—C11—C12	−0.2 (5)	C4—C5—C16—C17	−48.3 (4)
N2—C7—C12—C11	178.6 (2)	C3—C2—C17—C16	−56.1 (4)
C8—C7—C12—C11	−0.4 (3)	C1—C2—C17—C16	66.7 (5)
N2—C7—C12—C13	0.5 (2)	C5—C16—C17—C2	48.2 (5)

Comparison of Selected Torsion Angles (°)

Torsion Angle	**Ia**	**II**
C6—C13—C14—C15	-3.6 (7)	0.2 (4)
C13—C14—C15—N1	-47.8 (6)	-20.2 (3)

*Comparison of hydrogen-bond geometries for **II** and **Ia** (Å, °)*

Symmetry codes: (i) 3/2-x,-y,-1/2+z, (ii) x+1, y, z.

Structure	D—H···A	D—H	H···A	D···A	D—H···A
II	C6—H6···N1	0.93	2.31	2.851 (4)	116
	C4—H4···O1	0.98	2.44	2.803 (3)	109
	C11—H11···O1	0.93	2.59	3.086 (3)	114
	N2—H2N···O1^{i}	0.88 (3)	2.03 (3)	2.852 (2)	154 (3)
Ia	C6—H6···N1	0.93	2.52	2.966 (6)	109
	N2—H2N···O1^{ii}	0.88	2.50	2.968 (6)	112

Spectroscopic characterization of II by ^{1}H-NMR (CD_3OD, 600 MHz) and ^{13}C-NMR (CD_3OD, 150 MHz). (For site-codes see Fig.1)

Site	H (ppm)	C (ppm)	Site	H (ppm)	C (ppm)
1	-	60.3	11	8.28, m	123.0
2	1.90, t, 1.89	37.2	12	-	127.5
3	2.22, m 2.08, m	29.9	13	-	115.4
4	3.76, s	42.5	14	-	190.3
5	-	147.2	15	-	169.2
6	8.07, s	138.3	16	1.64, m 2.08, m	29.5
7	-	138.4	17	1.77, m 2.20, m	30.2
8	7.46, m	112.8	18	1.52	27.3
9	7.26, m	124.6	19	1.32	31.3
10	7.25, m	123.6	20	4.75, d, 1.7 4.70, d, 1.7	110.5