2·05 (4), O(7)···O(21) ($-x$, $y-\frac{1}{2}$, $\frac{1}{2}-z$) = 2·81 (1) Å, O(7)—H(7)···O(21) = 177 (4)°].

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References

BUCOURT, R. (1974). *Topics in Stereochemistry*, Vol. 8, edited by E. L. ELIEL & N. L. ALLINGER. New York: Interscience/Wiley.

CARSTENN-LICHTERFELDE, C. VON, PASCUAL, C., PONS, J., RABANAL, R. M., RODRIGUEZ, B. & VALVERDE, S. (1975). *Tetrahedron Lett.* **41**, 3569–3572.

CARSTENN-LICHTERFELDE, C. VON, VALVERDE, S. & RODRIGUEZ, B. (1974). *Aust. J. Chem.* **27**, 517–529.

CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.

CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.

GARCIA-GRANADOS, A., MARTINEZ, A., ONORATO, M. E. & SANTORO, J. (1986). *Magn. Reson. Chem.* **24**, 853–861.

GARCIA-GRANADOS, A., MARTINEZ, A., ONORATO, M. E. & SOCORRO, O. (1984). *Phytochemistry*, **23**, 607–610.

HALL, S. R. & MASLEN, E. N. (1965). *Acta Cryst.* **18**, 265–279.

HANSON, J. R., MCLAUGHLIN, G. M. & SIM, G. A. (1972). *J. Chem. Soc. Perkin Trans.* 2, pp. 1124–1130.

KUPCHAN, S. M., DAVIES, V. H., FUJITA, T., COX, M. R., RESTIVO, R. J. & BRYAN, R. F. (1973). *J. Org. Chem.* **38**, 1853–1858.

LEE, E. F. (1990). PhD dissertion. Univ. of Texas, Austin, Texas, USA.

MUIR, K. W. & SIM, G. A. (1968). *J. Chem. Soc. B*, pp. 667–673.

MURAKAMI, T., TANAKA, N., IIDA, H. & IITAKA, Y. (1981). *Chem. Pharm. Bull.* **29**, 773–778.

ROGERS, D. (1981). *Acta Cryst.* A**37**, 734–741.

SCHOMAKER, V. & TRUEBLOOD, K. N. (1968). *Acta Cryst.* B**24**, 63–76.

SEAMAN, F., BOHLMANN, F., ZDERO, C. & MABRY, T. J. (1989). *Diterpenes of Flowering Plants, Compositae (Asteraceae)*. New York: Springer-Verlag.

SHELDRICK, G. M. (1976). *SHELX76. Program for crystal structure determination*. Univ. of Cambridge, England.

SHELDRICK, G. M. (1987). *SHELXTL-Plus*. Release 3.4 for Nicolet *R3m/V* crystallographic system. Nicolet Instrument Corporation, Madison, Wisconsin, USA.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Phys. Chem.* **42**, 3175–3187.

TOROMANOFF, E. (1980). *Tetrahedron*, **36**, 2809–2931.

WATSON, W. H., TAVANAIEPOUR, I., LEE, E. F. & MABRY, T. J. (1986). *Acta Cryst.* C**42**, 1591–1594.

Acta Cryst. (1991). C**47**, 787–790

Structure of Two Polymorphs of 2-Methyl-3,4′-bipyridin-6(1*H*)-one

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Abstract. $C_{11}H_{10}N_2O$, $M_r = 186{\cdot}22$. Polymorph (I) monoclinic, $P2_1/c$, $a = 7{\cdot}574$ (1), $b = 11{\cdot}132$ (2), $c = 11{\cdot}437$ (2) Å, $\beta = 94{\cdot}90$ (1)°, $V = 960{\cdot}8$ (5) Å^3, $Z = 4$, $D_x = 1{\cdot}287$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}079$ mm^{-1}, $F(000) = 392$, $T = 293$ K, $R = 0{\cdot}058$ for 2335 observed reflections. Polymorph (II) monoclinic, $P2_1/c$, $a = 6{\cdot}7897$ (7), $b = 13{\cdot}449$ (2), $c = 10{\cdot}736$ (1) Å, $\beta = 108{\cdot}644$ (8)°, $V = 928{\cdot}9$ (2) Å^3, $Z = 4$, $D_x = 1{\cdot}331$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}082$ mm^{-1}, $F(000) = 392$, $T = 293$ K, $R = 0{\cdot}047$ for 1952 observed reflections. The molecular conformations in the two polymorphs are similar and the torsion angle C(2)—C(1)—C(1′)—C(2′) is 58·9 (2) and 54·1 (2)° for (I) and (II), respectively. Both structures contain centrosymmetric hydrogen-bonded dimers of molecules with the pyridone ring NH groups acting as donors and the keto O atoms as acceptors with N···O distances of 2·776 (2) and 2·765 (1) Å for (I) and (II), respectively.

Introduction. Bipyridine derivatives, a new class of nonglycosidic cardiac positive inotropic agents which inhibit phosphodiesterase isozyme III activity (Baim, McDowell, Cherniles, Monrad, Parker, Edelson, Braunwald & Grossman, 1983), have been developed for the treatment of congestive heart failure. The most potent inotropic agent in the series, milrinone (2-methyl-6-oxo-1,6-dihydro-3,4′-bipyridine-5-carbonitrile), also stimulates rabbit myocardial membrane Ca^{2+}ATPase activity *in vitro* in a way similar to that of thyroid hormones (Mylotte, Cody, Davis, Davis, Blas & Schoenl, 1985). Milrinone, revealing structural homology to thyroxine (Cody, 1987), competes with thyroid hormones for their binding sites on human serum transthyretin (thyroxine-binding prealbumin) (Davis, Cody, Davis, Warnick, Schoenl & Edwards, 1987). We have determined the struc-

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Table 1. *Atomic fractional coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($\times 10^2$) *with e.s.d.'s for polymorphs* (I) *and* (II)

$B_{eq} = (8\pi^2/3)\sum_i\sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}(Å^2)
(I)				
C(1)	3951 (2)	8619 (1)	3274 (1)	307 (3)
C(2)	3317 (2)	9282 (1)	2317 (1)	295 (3)
C(4)	5999 (2)	8911 (1)	1331 (1)	329 (3)
C(5)	6654 (2)	8227 (1)	2329 (1)	392 (4)
C(6)	5659 (2)	8102 (1)	3257 (1)	375 (3)
C(21)	1575 (2)	9914 (2)	2171 (2)	415 (4)
C(1′)	2898 (2)	8422 (1)	4296 (1)	314 (3)
C(2′)	1258 (2)	7877 (2)	4175 (1)	442 (4)
C(3′)	325 (2)	7713 (2)	5154 (1)	503 (5)
C(5′)	2500 (3)	8574 (1)	6343 (1)	444 (4)
C(6′)	3548 (2)	8751 (1)	5425 (1)	403 (4)
N(3)	4356 (1)	9408 (1)	1404 (1)	312 (3)
N(4′)	895 (2)	8076 (1)	6229 (1)	446 (3)
O(4)	6801 (1)	9079 (1)	434 (1)	440 (3)
(II)				
C(1)	6166 (2)	1358 (1)	1822 (1)	296 (3)
C(2)	6663 (2)	602 (1)	2727 (1)	294 (3)
C(21)	8341 (3)	−153 (1)	2887 (2)	430 (5)
N(3)	5621 (2)	530 (1)	3621 (1)	292 (3)
C(4)	4089 (2)	1161 (1)	3713 (1)	295 (3)
O(4)	3250 (2)	1009 (1)	4584 (1)	384 (3)
C(5)	3591 (2)	1948 (1)	2786 (1)	364 (4)
C(6)	4607 (2)	2038 (1)	1881 (1)	356 (4)
C(1′)	7229 (2)	1481 (1)	818 (1)	306 (3)
C(2′)	7300 (3)	731 (1)	−50 (2)	391 (4)
C(3′)	8282 (3)	894 (1)	−974 (1)	440 (5)
N(4′)	9247 (2)	1735 (1)	−1084 (1)	422 (4)
C(5′)	9182 (3)	2454 (1)	−245 (1)	399 (4)
C(6′)	8187 (2)	2371 (1)	691 (1)	356 (4)

Table 2. *Bond lengths* (Å) *and bond angles* (°) *with e.s.d.'s for polymorphs* (I) *and* (II)

	(I)	(II)
C(1)—C(2)	1·373 (2)	1·372 (2)
C(1)—C(6)	1·418 (2)	1·416 (2)
C(1)—C(1′)	1·487 (2)	1·487 (2)
C(2)—N(3)	1·367 (2)	1·365 (2)
C(2)—C(21)	1·492 (2)	1·495 (2)
N(3)—C(4)	1·370 (2)	1·371 (2)
C(4)—C(5)	1·425 (2)	1·418 (2)
C(4)—O(4)	1·251 (2)	1·257 (2)
C(5)—C(6)	1·361 (2)	1·366 (2)
C(1′)—C(2′)	1·379 (2)	1·386 (2)
C(1′)—C(6′)	1·391 (2)	1·389 (2)
C(2′)—C(3′)	1·386 (2)	1·378 (3)
C(3′)—N(4′)	1·330 (2)	1·330 (2)
N(4′)—C(5′)	1·333 (2)	1·333 (2)
C(5′)—C(6′)	1·384 (2)	1·383 (3)
	(I)	(II)
C(2)—C(1)—C(6)	117·7 (1)	117·8 (2)
C(2)—C(1)—C(1′)	122·1 (1)	122·0 (1)
C(6)—C(1)—C(1′)	120·1 (1)	120·2 (1)
C(1)—C(2)—N(3)	118·6 (1)	119·0 (1)
C(1)—C(2)—C(21)	126·0 (1)	126·2 (1)
N(3)—C(2)—C(21)	115·4 (1)	114·7 (1)
C(2)—N(3)—C(4)	126·2 (1)	125·6 (1)
N(3)—C(4)—C(5)	115·0 (1)	115·4 (1)
N(3)—C(4)—O(4)	119·8 (1)	119·2 (1)
C(5)—C(4)—O(4)	125·2 (1)	125·5 (1)
C(4)—C(5)—C(6)	120·1 (1)	120·3 (1)
C(1)—C(6)—C(5)	122·4 (1)	122·0 (1)
C(1)—C(1′)—C(2′)	121·7 (1)	122·4 (1)
C(1)—C(1′)—C(6′)	121·3 (1)	121·2 (1)
C(2′)—C(1′)—C(6′)	117·0 (1)	116·3 (1)
C(1′)—C(2′)—C(3′)	119·6 (1)	119·8 (1)
C(2′)—C(3′)—N(4′)	124·0 (1)	124·4 (1)
C(3′)—N(4′)—C(5′)	116·0 (1)	115·7 (1)
N(4′)—C(5′)—C(6′)	124·2 (1)	124·2 (1)
C(1′)—C(6′)—C(5′)	119·1 (1)	119·6 (1)

tures of milrinone and several of its analogues (Cody, 1987; Cody, Suwińska & Wojtczak, 1990) in order to delineate features essential for their biological activity. Here we report the structure of two polymorphs of 2-methyl-3,4′-bipyridin-6(1*H*)-one which does not stimulate Ca^{2+}-ATPase in this assay system.

Experimental. Samples were obtained from Sterling–Winthrop. Crystals of (I) from EtOH, of (II) from toluene/MeOH solution; cell parameters from 25 reflections $20{\cdot}23 < 2\theta < 30{\cdot}01°$ (I), 50 reflections $25{\cdot}87 < 2\theta < 35{\cdot}10°$ for (II); Syntex *P*3 diffractometer; Nb filter, Mo $K\alpha$ radiation; ω–2θ scan; 4010 reflections $4 < 2\theta < 60°$ ($-1 < h < 10$, $0 < k < 16$, $-17 < l < 17$) measured for $0{\cdot}20 \times 0{\cdot}74 \times 0{\cdot}80$ mm crystal of (I); 3186 reflections $4 < 2\theta < 55°$ ($-1 < h < 9$, $0 < k < 18$, $-14 < l < 14$) for $0{\cdot}3 \times 0{\cdot}4 \times 0{\cdot}5$ mm crystal of (II); 6 standards measured every 90 reflections for (I) and 6 standards measured every 60 reflections for (II) revealed no significant intensity variation, no absorption and extinction corrections; 2841 unique reflections of which 2335 observed $I > 3\sigma(I)$ for (I), 2150 unique and 1952 observed reflections $I > 3\sigma(I)$ for (II); direct methods used *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) and *NQEST* (De Titta, Edmonds, Langs & Hauptman, 1975), $\sum w(|F_o| - |F_c|)^2$ minimized in full-matrix least squares. For both structures H-atom positions from the difference map, anisotropic refinement of non-H atoms and isotropic refinement of H atoms, $w = 1/\sigma^2(F)$ for (I) and (II). Final $|\Delta/\sigma| < 0{\cdot}01$, $\Delta\rho_{max} = 0{\cdot}33$ and $\Delta\rho_{min} = -0{\cdot}37$ e Å^{-3} for (I); $|\Delta/\sigma| < 0{\cdot}09$, $\Delta\rho_{max} = 0{\cdot}28$ and $\Delta\rho_{min} = -0{\cdot}31$ e Å^{-3} for (II). Final $R = 0{\cdot}058$, $wR = 0{\cdot}070$ and $S = 2{\cdot}610$ for (I), $R = 0{\cdot}047$, $wR = 0{\cdot}077$ and $S = 3{\cdot}899$ for (II). Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV). Other data processing programs described by Blessing (1989) and from the Enraf–Nonius package (Enraf–Nonius, 1979) run on a VAX8600 computer.

Discussion. Fractional atomic coordinates for (I) and (II) are listed in Table 1,* bond distances and angles in Table 2 and hydrogen bonds and close contact

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and best planes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53404 (41 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *Hydrogen-bond geometry and close contacts in* (I) *and* (II)

Hydrogen-bond geometry in polymorph (I) structure

D—H···*A* (symmetry code)	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H—*A* (°)
N(3)—H(3)···O(4) (1 − *x*, 2 − *y*, −*z*)	0·903 (17)	1·873 (17)	2·776 (2)	180 (1)

Hydrogen-bond geometry in polymorph (II) structure

D—H···*A* (symmetry code)	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H—*A* (°)
N(3)—H(3)···O(4) (1 − *x*, −*y*, 1 − *z*)	0·930 (18)	1·836 (18)	2·765 (1)	176 (1)

Close intermolecular interactions in polymorphs (I) and (II) (Å)

(I)		(II)	
C(1)···C(5′)^{i}	3·410 (2)	C(2)···C(5′)^{iii}	3·482 (2)
C(2)···C(5′)^{i}	3·409 (2)	O(4)···C(21)^{iv}	3·426 (2)
C(2)···N(4′)^{i}	3·379 (2)		
O(4)···C(3′)^{ii}	3·369 (2)		

Symmetry operators: (i) x, $1{\cdot}5 - y$, $-0{\cdot}5 + z$; (ii) $1 + x$, $1{\cdot}5 - y$, $-0{\cdot}5 + z$; (iii) x, $0{\cdot}5 - y$, $0{\cdot}5 + z$; (iv) $1 - x$, $-y$, $1 - z$.

geometry in Table 3. The molecular conformation and packing diagrams are shown in Figs. 1 and 2, respectively. There is a small difference between the conformation of the two polymorphs: the torsion angle [C(2)—C(1)—C(1′)—C(2′)] between the two rings is 58·9 (3) and 54·1 (2)° for (I) and (II), respectively. These values are larger than those for milrinone [42·4 (8)°; Cody, 1987] but smaller than for N^3-methyl milrinone free base [66·6 (2)°; Cody, Suwińska & Wojtczak, 1990].

There are small differences in the bond lengths and angles of these polymorphic structures (Table 3). The pyridone ring in both structures is planar and the mean deviations from the best planes are 0·006 and 0·003 Å for (I) and (II), respectively. The difference observed in the pyridone ring geometry of these polymorphs and that of milrinone, *i.e.* an increase in C(4)—O(4) and decrease in both C(4)—C(5) and C(5)—C(6), is a reflection of the electron-withdrawing effects of the 5-cyano group of milrinone, not present in these polymorphs.

The crystal packing in the two polymorphs is similar with the bipyridine molecules forming centrosymmetric hydrogen-bonded dimers (Table 3) in alternate layers in the [101] direction (Fig. 2) and ring–ring stacking interactions in alternate layers parallel to the *c* axis. Additionally, the packing patterns are tilted relative to one another such that the hydrogen-bonded dimers in (I) are more nearly parallel to the *b* axis than in (II). The structure of (I) contains a larger number of close contacts than (II). In spite of this, the conformational differences between (I) and (II) reflect the smaller crystal density of polymorph (I).

Earlier structure–activity data for this series of inotropic bipyridines revealed that the minimal requirements for Ca^{2+}-ATPase stimulation were the presence of a 2-methyl group which results in a twist conformation about the bipyridine bridge and an electronegative substituent in position 5. The inactivity of this analog is in agreement with this model as it confirms the greater importance of an appropriate 5-substituent than the conformational influence of the 2-methyl group.

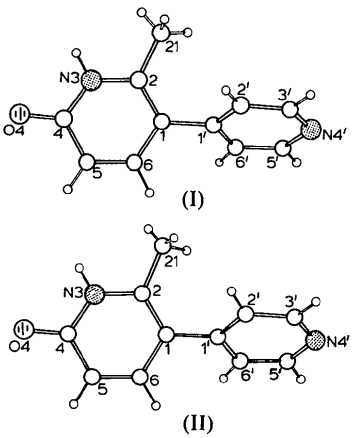

Fig. 1. Molecular conformation of polymorphs (I) and (II) of 2-methyl-3,4′-bipyridin-6(1*H*)-one with numbering scheme.

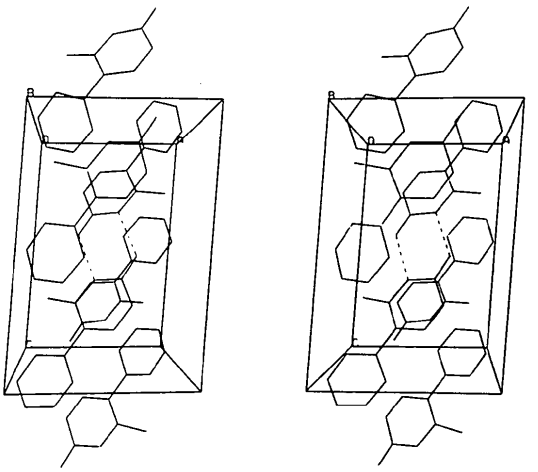

Fig. 2. Stereoview of the packing diagram of polymorph (I). Hydrogen bonds are indicated by broken lines. **a** is horizontal, **b** is in the plane of the paper and **c** is vertical.

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References

BAIM, D. S., MCDOWELL, A. V., CHERNILES, J., MONRAD, E. S., PARKER, J. A., EDELSON, J., BRAUNWALD, E. & GROSSMAN, W. (1983). *N. Engl. J. Med.* **309**, 748–756.

BLESSING, R. H. (1989). *J. Appl. Cryst.* **22**, 396–397.

CODY, V. (1987). *Acta Cryst.* C**43**, 1325–1328.

CODY, V., SUWIŃSKA, K. & WOJTCZAK, A. (1990). *Acta Cryst.* C**47**. 156–159.

DAVIS, P. J., CODY, V., DAVIS, F. B., WARNICK, P. R., SCHOENL, M. & EDWARDS, L. (1987). *Biochem. Pharmacol.* **36**, 3635–3640.

DE TITTA, G. T., EDMONDS, J. W., LANGS, D. A. & HAUPTMAN, H. A. (1975). *Acta Cryst.* A**31**, 472–479.

Enraf–Nonius (1979). *Structure Determination Package*. Enraf–Nonius, Delft, The Netherlands.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN*78. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

MYLOTTE, K. M., CODY, V., DAVIS, P. J., DAVIS, F. B., BLAS, S. D. & SCHOENL, M. (1985). *Proc. Natl Acad. Sci. USA*, **82**, 7974–7978.

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Structure of a New Dammarane-type Triterpene* from *Gynostemma pentaphyllum* (Thurb.) Makino

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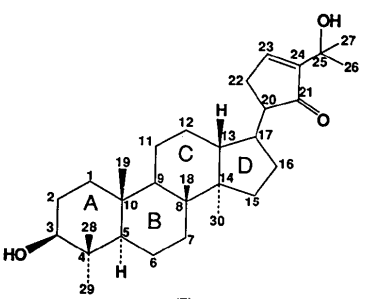
Abstract. $C_{30}H_{48}O_3$, $M_r = 456{\cdot}7$, monoclinic, $C2$, $a = 35{\cdot}515\ (2)$, $b = 6{\cdot}758\ (1)$, $c = 11{\cdot}116\ (1)$ Å, $\beta = 97{\cdot}59\ (1)°$, $V = 2644{\cdot}6\ (8)$ Å^3, D_m(flotation) = 1·153 (5), $D_x = 1{\cdot}147$ Mg m^{-3}, $Z = 4$, $F(000) = 1008$, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 0{\cdot}48$ mm^{-1}, $T = 290\ (1)$ K. Final $R = 0{\cdot}042$ for 2346 observed data. The molecular structure is based on a tetracyclic triterpenoid skeleton of the dammarane type and is a diol with the dammarane side chain modified to a cyclopentenone moiety. Intermolecular hydrogen bonds involving both hydroxyl groups link the molecules into double layers parallel to the *ab* plane in the crystal.

Introduction. *Gynostemma pentaphyllum* (Thurb.) Makino (family Cucurbitaceae) is a perennial creeping herb widely distributed in China, Japan, Korea and southeast Asia. It was used as a sweetener in Japan and has been used as a folk medicine in China for relieving inflammation and coughs, as an expectorant and for treating chronic bronchitis and infectious hepatitis (Zhou, 1988). Studies on its chemical constituents were begun by Nagai, Nagumo & Izawa (1976) and now more than 80 dammarane-type saponins (gynpenosides) have been isolated and identified. Several of these were identified as ginsenosides previously isolated from *Panax ginseng* C. A. Meyer (Ollis & Shibata, 1986), a well known traditional Chinese medicine. Because of their biological activities, much attention is now focused on gynpenosides.

Acid hydrolysis of a glycoside mixture from *Gynostemma pentaphyllum* (Thurb.) Makino from Yunnan China locations yielded three aglycones, one of these being the gynogenin reported here. Subsequent ^{13}C NMR and mass-spectral data indicated that the latter has a molecular structure based on a tetracyclic triterpenoid skeleton of dammarane type, but the NMR data showed it to differ from other known dammarane-type sapogenins. An X-ray analysis has now defined the molecular structure of this hitherto unknown gynogenin as (I).



(I)

* (20*R*)-3β,25-Dihydroxy-21,24-cyclo-dammar-23-en-21-one.

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