O(2)—C(2)—N	122.0 (3)	C(8)—C(8a)—Se	116.8 (2)
O(2)—C(2)—Se	117.0 (3)	C(14)—C(9)—C(10)	121.2 (3)
N—C(2)—Se	121.0 (2)	C(14)—C(9)—N	118.6 (3)
O(4)—C(4)—N	117.6 (3)	C(10)—C(9)—N	120.2 (3)

The structure was solved by the heavy-atom method using *SHELXS*86 (Sheldrick, 1990). Refinement was performed by *SHELXL*93 (Sheldrick, 1993) using full-matrix least squares, with anisotropic displacement parameters for all non-H atoms. H atoms were included at calculated positions and refined using a riding model with isotropic displacement parameters assigned. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*93.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry and least-squares-planes data have been deposited with the IUCr (Reference: KH1013). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Esker, J. H. & Newcomb, M. (1994). *J. Org. Chem.* **59**, 2779–2786.
Fong, M. C. & Schiesser, C. H. (1995). *Aust. J. Chem.* In the press.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Kitano, Y., Kashiwagi, M. & Kinoshita, Y. (1972). *Acta Cryst.* B**28**, 1223–1231.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1993). *SHELXL93. Program for Crystal Structure Refinement*. Univ. of Göttingen, Germany.

Acta Cryst. (1995). C**51**, 1335–1338

Three Polymorphic Forms of 2-Ethyl-3-hydroxy-4-pyranone (Ethyl Maltol)

Simon D. Brown, John Burgess, John Fawcett,
Simon A. Parsons, David R. Russell and
Emma Waltham

Department of Chemistry, University of Leicester, Leicester LE1 7RH, England

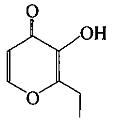
(*Received* 9 *September* 1994; *accepted* 6 *December* 1994)

Abstract

The crystal structures of three polymorphic forms of ethyl maltol (2-ethyl-3-hydroxy-4-pyranone), $C_7H_8O_3$, have been determined. The polymorphs exhibit different molecular arrangements through intermolecular hydrogen bonding. Form (1) contains nearly planar chains of molecules, (2) contains three-dimensional or spiral chains and (3) contains hydrogen-bonded dimers.

Comment

Pyranones are biologically important chelating ligands which may be used for removing metal overloads from the body or the introduction of metals for therapy or NMR imaging (Hider & Hall, 1991; Burgess, 1993). Maltol (3-hydroxy-2-methyl-4-pyranone) is a naturally occurring pyranone much used in the baking industry. The ethyl analogue of maltol has been found in three polymorphic forms, all of which were crystallized as minor components; polymorph (1) was isolated from the attempted reaction between crude 3-benzyloxy-2-ethyl-4-pyranone and 4-fluoroaniline while (2) and (3) were obtained from preparations of the metal complexes of Si and Sb, respectively. This is not unexpected, as the potential of these compounds as drug-transport systems depends on the very similar solubilities of the ligand and the metal complexes.



Ethyl Maltol

In each of the structures the hydroxyl H atom H(1) bonded to O(1) is involved in intermolecular hydrogen bonding to a terminal carbonyl O atom O(2). In polymorphs (1) and (2) the hydrogen bonds link the molecules to form infinite chains. In the case of polymorph (1) the result is a near-planar chain (Fig. 1) in which adjacent molecules are related by a crystallographic twofold screw axis. Polymorph (2) contains a three-dimensional chain (Fig. 2) in which adjacent molecules spiral along a crystallographic threefold screw axis. In polymorph (3) pairs of molecules form hydrogen-bonded dimers mutually linked across a crystallographic centre of symmetry (Fig. 3). In all three forms the H atom H(1) was located as the highest residual electron-density peak after all other atoms were included in the refinement (other H atoms were included in calculated positions) and was subsequently included in a riding position in the final least-squares cycles. The intermolecular contact distances between the hydroxyl O atoms O(1) and O(2) (Table 2) are similar [2.724 (4), 2.676 (1) and 2.711 (2) Å for the polymorphic forms (1), (2) and (3), respectively] and are consistent with hydrogen bonding. Although the positions of the bridging H atoms were not refined, their locations are chemically reasonable, with H(1)···O(2) distances of 1.89, 1.87 and 1.81 Å and O(1)—H(1)···O(2) angles of 146, 155 and 152° for forms (1), (2) and (3), respectively.

Maltol (3-hydroxy-2-methyl-4-pyranone) has also been found in two polymorphic forms (Burgess, Fawcett, Llewellyn & Russell, 1995), one of which contains a planar chain similar to that found in (1) and the

Acta Crystallographica Section C
ISSN 0108-2701 ©1995

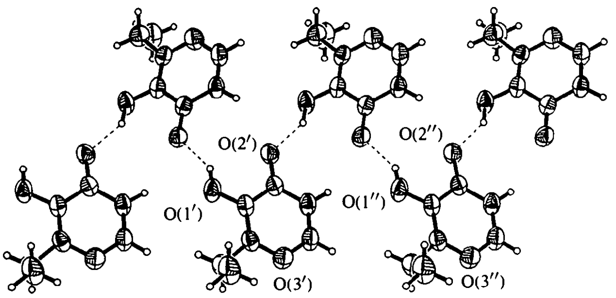


Fig. 1. Structure of polymorph (1) (*SHELXTL/PC XP*; Sheldrick, 1990) showing the near-planar chain of hydrogen-bonded molecules about a crystallographic 2_1 axis. Intermolecular hydrogen bonds are indicated by the broken lines. Displacement ellipsoids are drawn at the 50% probability level for all three polymorphs.

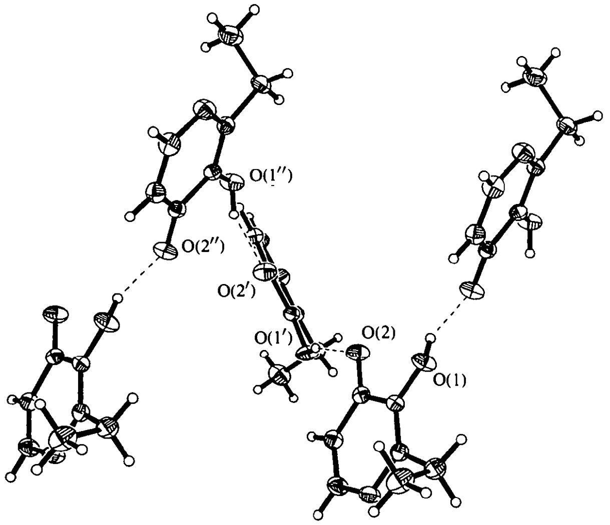


Fig. 2. Structure of polymorph (2) (*SHELXTL/PC XP*; Sheldrick, 1990) showing the spiral arrangement of the hydrogen-bonded molecules around a crystallographic 3_1 axis.

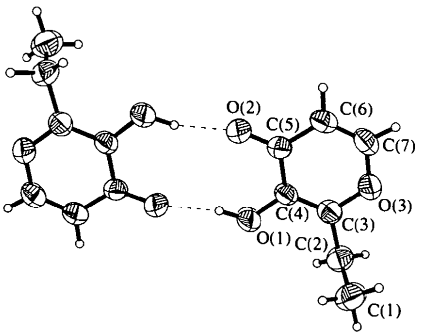


Fig. 3. Structure of polymorph (3) (*SHELXTL/PC XP*; Sheldrick, 1990) showing the hydrogen-bonded dimeric pairs of molecules. The atom-labelling scheme is common to all three polymorphs.

other having a dimeric structure where the dimers exhibit identical bridging to that found in (3).

The analogous pyridinone compounds display similar hydrogen-bonded structures. 1,2-Dimethyl-3-hydroxy-4-pyridone has been reported as forming centrosymmetric dimers (Hider, Taylor, Walkinshaw, Wang & van der Helm, 1990; Chan, Ghosh, Venkataram, Rahman & Grant, 1992), as has 1-ethyl-2-methyl-3-hydroxy-4-pyridinone (EMHP) (Xiao, van der Helm, Hider & Dobbin, 1992). In all of these structures the hydroxyl H atoms have been located in the plane occupied by the pyranone or pyridinone ring and O atoms and inclined towards the O(2) atom of the same molecule, suggesting a very weak intramolecular interaction. In the structure of 1,2-diethyl-3-hydroxy-4-pyridone pairs of molecules also form dimers, like the dimeric structures described above (Burgess, Fawcett, Patel & Russell, 1993).

In view of the polymorphic forms reported here for ethyl maltol and the analogous methyl maltol and pyridones, it is likely that further forms of some or all of these compounds will be found.

Experimental

Polymorph (1) was isolated as a white solid from the attempted reaction between crude 3-benzyloxy-2-ethyl-4-pyranone and 4-fluoroaniline. Crystals were grown from ethanol/water (50:50). Polymorph (2) was obtained as a minor unreacted component from the preparation of $Si(etmalt)_2Cl_2$ (etmalt = ethyl maltol). Silicon tetrachloride (0.85 g, 5 mmol) was added dropwise to a stirred solution of ethyl maltol (1.4 g, 10 mmol) in 25 ml of anhydrous CH_2Cl_2. A white precipitate was formed, which was washed with diethyl ether. Crystals we obtained by fractional crystallization. Polymorph (3) was obtained as a minor unreacted component from the preparation of $Sb(etmalt)_3$. Aqueous 2 *M* NaOH was added to a methanol solution of antimony trichloride (0.5 g, 2.2 mmol) and ethyl maltol (0.92 g, 6.6 mmol) and the solution concentrated to a white solid. Crystal were obtained from hot methanol/water by fractional crystallization.

Polymorph (1)

Crystal data

$C_7H_8O_3$
$M_r = 140.1$
Monoclinic
$P2_1/n$
$a = 4.867\,(2)$ Å
$b = 6.895\,(2)$ Å
$c = 20.200\,(6)$ Å
$\beta = 95.23\,(1)°$
$V = 675.0\,(4)$ Å^3
$Z = 4$
$D_x = 1.379$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 30 reflections
$\theta = 6.9$–$12.5°$
$\mu = 0.108$ mm^{-1}
$T = 293$ K
Block
0.78 × 0.34 × 0.17 mm
Colourless

Data collection

Siemens *P*4 diffractometer
ω scans
Absorption correction: none

$\theta_{\max} = 25°$
$h = -1 \rightarrow 5$
$k = -1 \rightarrow 8$
$l = -23 \rightarrow 24$

1760 measured reflections
1100 independent reflections
715 observed reflections $[F > 4\sigma(F)]$
$R_{\text{int}} = 0.0389$
3 standard reflections monitored every 100 reflections intensity decay: 1%

Refinement

Refinement on F
$R = 0.077$
$wR = 0.104$
$S = 1.83$
715 reflections
91 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F) + 0.0015F^2]$
$(\Delta/\sigma)_{\text{max}} = 0.005$
$\Delta\rho_{\text{max}} = 0.30$ e Å^{-3}
$\Delta\rho_{\text{min}} = -0.24$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C)

Polymorph (2)

Crystal data

$C_7H_8O_3$
$M_r = 140.1$
Rhombohedral
$R\bar{3}$ (hexagonal axes)
$a = 20.828$ (3) Å
$c = 7.832$ (2) Å
$V = 2942$ (1) Å^3
$Z = 18$
$D_x = 1.423$ Mg m^{-3}
Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 27 reflections
$\theta = 5.4$–$12.4°$
$\mu = 0.112$ mm^{-1}
$T = 293$ K
Plate
0.43 × 0.36 × 0.18 mm
Colourless

Data collection

Siemens $P4$ diffractometer
ω scans
Absorption correction: none
5053 measured reflections
1425 independent reflections
1024 observed reflections $[F > 4\sigma(F)]$
$R_{\text{int}} = 0.0165$
$\theta_{\text{max}} = 22.5°$
$h = -26 \rightarrow 26$
$k = -26 \rightarrow 26$
$l = -9 \rightarrow 1$
3 standard reflections monitored every 100 reflections intensity decay: 2%

Refinement

Refinement on F
$R = 0.0408$
$wR = 0.057$
$S = 1.21$
1024 reflections
91 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F) + 0.0013F^2]$
$(\Delta/\sigma)_{\text{max}} = 0.001$
$\Delta\rho_{\text{max}} = 0.18$ e Å^{-3}
$\Delta\rho_{\text{min}} = -0.18$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C)

Polymorph (3)

Crystal data

$C_7H_8O_3$
$M_r = 140.1$
Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Triclinic
$P\bar{1}$
$a = 7.144$ (3) Å
$b = 7.641$ (2) Å
$c = 7.700$ (4) Å
$\alpha = 62.13$ (1)°
$\beta = 68.28$ (1)°
$\gamma = 76.39$ (1)°
$V = 344.2$ (3) Å^3
$Z = 2$
$D_x = 1.352$ Mg m^{-3}
Cell parameters from 19 reflections
$\theta = 5.5$–$12.4°$
$\mu = 0.106$ mm^{-1}
$T = 293$ K
Plate
0.58 × 0.41 × 0.18 mm
Colourless

Data collection

Siemens $P4$ diffractometer
ω scans
Absorption correction: none
1771 measured reflections
1431 independent reflections
813 observed reflections $[F > 4\sigma(F)]$
$R_{\text{int}} = 0.0182$
$\theta_{\text{max}} = 27°$
$h = -1 \rightarrow 9$
$k = -8 \rightarrow 8$
$l = -9 \rightarrow 9$
3 standard reflections monitored every 100 reflections intensity decay: 2%

Refinement

Refinement on F
$R = 0.0519$
$wR = 0.0733$
$S = 1.10$
813 reflections
91 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F) + 0.0029F^2]$
$(\Delta/\sigma)_{\text{max}} = 0.002$
$\Delta\rho_{\text{max}} = 0.19$ e Å^{-3}
$\Delta\rho_{\text{min}} = -0.29$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$$U_{\text{eq}} = (1/3)\Sigma_i\Sigma_jU_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
Polymorph (1)				
O(1)	0.0753 (9)	0.1371 (5)	0.3406 (2)	0.063 (1)
O(2)	0.1946 (8)	0.4397 (5)	0.2573 (2)	0.062 (1)
O(3)	−0.3677 (8)	0.5139 (5)	0.3918 (2)	0.062 (1)
C(1)	−0.1863 (16)	0.2443 (9)	0.5070 (2)	0.079 (2)
C(2)	−0.3150 (14)	0.1974 (8)	0.4379 (2)	0.064 (2)
C(3)	−0.2333 (2)	0.3404 (7)	0.3875 (2)	0.052 (2)
C(4)	−0.0470 (12)	0.3134 (7)	0.3428 (2)	0.049 (2)
C(5)	0.0206 (11)	0.4667 (7)	0.2986 (2)	0.048 (2)
C(6)	−0.1167 (12)	0.6457 (7)	0.3070 (2)	0.053 (2)
C(7)	−0.3051 (14)	0.6586 (8)	0.3510 (2)	0.064 (2)
Polymorph (2)				
O(1)	0.4739 (1)	0.1203 (1)	0.0639 (2)	0.047 (1)
O(2)	0.3898 (1)	−0.0075 (1)	0.2488 (2)	0.048 (1)
O(3)	0.6074 (1)	0.0683 (1)	0.1774 (2)	0.045 (1)
C(1)	0.6825 (1)	0.2319 (1)	0.1286 (3)	0.061 (1)
C(2)	0.6284 (1)	0.1708 (1)	0.0123 (3)	0.046 (1)
C(3)	0.5750 (1)	0.1045 (1)	0.1074 (2)	0.036 (1)
C(4)	0.5026 (1)	0.0805 (1)	0.1311 (2)	0.033 (1)
C(5)	0.4564 (1)	0.0147 (1)	0.2275 (2)	0.034 (1)
C(6)	0.4947 (1)	−0.0206 (1)	0.2947 (3)	0.040 (1)
C(7)	0.5663 (1)	0.0070 (1)	0.2687 (3)	0.045 (1)
Polymorph (3)				
O(1)	0.9536 (3)	0.8984 (3)	0.3314 (3)	0.063 (1)
O(2)	0.7702 (3)	0.9633 (3)	0.0471 (3)	0.067 (1)
O(3)	0.4772 (3)	0.6941 (3)	0.6553 (3)	0.062 (1)

C(1)	0.8409 (6)	0.4850 (5)	0.8339 (5)	0.079 (2)
C(2)	0.7483 (5)	0.6929 (5)	0.7665 (4)	0.061 (2)
C(3)	0.6675 (4)	0.7501 (4)	0.5920 (4)	0.050 (1)
C(4)	0.7665 (4)	0.8418 (4)	0.3888 (4)	0.046 (1)
C(5)	0.6765 (4)	0.8810 (4)	0.2331 (4)	0.047 (1)
C(6)	0.4766 (4)	0.8202 (4)	0.3112 (5)	0.056 (2)
C(7)	0.3878 (4)	0.7337 (5)	0.5117 (5)	0.062 (2)

Table 2. *Selected geometric parameters* (Å, °)

	(1)	(2)	(3)
O(1)—C(4)	1.356 (6)	1.347 (3)	1.351 (4)
O(2)—C(5)	1.256 (6)	1.235 (2)	1.241 (3)
O(3)—C(3)	1.370 (6)	1.355 (3)	1.363 (4)
O(3)—C(7)	1.346 (6)	1.334 (2)	1.356 (5)
C(1)—C(2)	1.512 (7)	1.511 (3)	1.489 (5)
C(2)—C(3)	1.497 (7)	1.471 (2)	1.495 (5)
C(3)—C(4)	1.349 (7)	1.344 (3)	1.352 (3)
C(4)—C(5)	1.441 (6)	1.434 (2)	1.444 (5)
C(5)—C(6)	1.421 (7)	1.428 (3)	1.425 (4)
C(6)—C(7)	1.337 (8)	1.318 (3)	1.320 (4)
O(1)···O(2^{i})	2.724 (4)	2.676 (1)	2.711 (2)
C(3)—O(3)—C(7)	118.2 (4)	119.3 (2)	119.1 (2)
C(1)—C(2)—C(3)	111.9 (5)	112.4 (2)	111.8 (4)
O(3)—C(3)—C(2)	112.0 (4)	112.0 (2)	113.2 (2)
O(3)—C(3)—C(4)	121.1 (4)	121.1 (2)	120.3 (3)
C(2)—C(3)—C(4)	126.9 (5)	126.9 (2)	126.5 (3)
O(1)—C(4)—C(3)	118.0 (4)	118.5 (2)	118.8 (3)
O(1)—C(4)—C(5)	120.8 (4)	120.2 (2)	119.6 (2)
C(3)—C(4)—C(5)	121.3 (4)	121.3 (2)	121.6 (3)
O(2)—C(5)—C(4)	120.6 (4)	121.3 (2)	120.8 (3)
O(2)—C(5)—C(6)	124.1 (4)	124.7 (2)	124.4 (3)
C(4)—C(5)—C(6)	115.2 (4)	114.0 (2)	114.8 (2)
C(5)—C(6)—C(7)	119.7 (5)	121.3 (2)	120.5 (4)
O(3)—C(7)—C(6)	124.4 (5)	123.1 (2)	123.7 (3)

Symmetry codes: for polymorph (1), (i) $\frac{1}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$; for polymorph (2), (i) $\frac{1}{3}-y, -\frac{1}{3}-y+x, z-\frac{1}{3}$; for polymorph (3), (i) $2-x, 2-y, -z$.

The structures were solved by direct methods and refined by full-matrix least squares. H atoms bonded to C atoms were included in calculated positions (C—H 0.96 Å). With all non-H atoms refined with anisotropic displacement parameters the hydroxyl H atom H(1) was located as the highest residual electron-density peak and was included in the final cycles of least squares riding on atom O(1). All crystals of polymorph (1) gave broad, weak diffraction peaks, resulting in a small observed data set and consequent high value of *R*. Cell refinement and data collection: *XSCANS* (Fait, 1991). Data reduction, structure solution and refinement: *SHELXTL/PC* (Sheldrick, 1990). Molecular graphics: *SHELXTL/PC*.

Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the IUCr (Reference: AS1151). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Burgess, J. (1993). *Transition Met. Chem.* **18**, 439–448.
Burgess, J., Fawcett, J., Llewellyn, M. A. & Russell, D. R. (1995). In preparation.
Burgess, J., Fawcett, J., Patel, M. S. & Russell, D. R. (1993). *J. Chem. Res.* (*S*), pp. 50–51, *J. Chem. Res.* (*M*), 0214.
Chan, H.-K., Ghosh, S., Venkataram, S., Rahman, Y.-E. & Grant, D. J. W. (1992). *J. Pharm. Sci.* **81**, 353–358.
Fait, J. (1991). *XSCANS User's Manual.* Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Hider, R. C. & Hall, A. D. (1991). *Prog. Med. Chem.* **28**, 41–173.
Hider, R. C., Taylor, P. D., Walkinshaw, M., Wang, J. L. & van der Helm, D. (1990). *J. Chem. Res.* (*S*), p. 316; *J. Chem. Res.* (*M*), p. 2520.
Sheldrick, G. M. (1990). *SHELXTL/PC User's Manual.* Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Xiao, G. Y., van der Helm, D., Hider, R. C. & Dobbin, P. S. (1992). *J. Chem. Soc. Trans.* **22**, 3265–3271.

Acta Cryst. (1995). C**51**, 1338–1341

Hydrogen-Bonding Stabilization of *N*-Methyldopamine 4-*O*-Dihydrogenphosphate in HCl Acidic Solution: Synthesis of Z2055, a New Dopaminergic Prodrug

Sandra Ianelli and Mario Nardelli*

Dipartimento di Chimica Generale ed Inorganica,
Chimica Analitica, Chimica Fisica, Università degli
Studi di Parma, Centro di Studio per la Strutturistica
Diffrattometrica del CNR, Viale delle Scienze 78,
I-43100 Parma, Italy

Franco Doggi, Gabriele Norcini and
Francesco Santangelo

Medicinal Chemistry Department, R&D Division,
Zambon Group Spa, Via Lillo del Duca 10, I-20091
Milano, Italy

(*Received* 5 *December* 1994; *accepted* 19 *December* 1994)

Abstract

The crystal structure analysis of 4-[2-(methylamino)-ethyl]-1,2-benzenediol 1-(dihydrogenphospate) hydrochloride, $C_9H_{15}NO_5P^{+}.Cl^{-}$, shows that the Cl^{-} ion is an acceptor in a hydrogen-bonding system joining the ammonium cations in endless chains and involving one phosphate and the phenol hydroxyl groups together with the ammonium group, acting as proton donors. The stability of this system may justify the isomerization of the 4-hydroxy-3-*O*-phosphate to 3-hydroxy-4-*O*-phosphatephenethyl moiety, observed in strongly acidic HCl solution. This isomerization allows simplification of the synthesis of the Z2055 dopaminergic prodrug.

Comment

Dopamine [DA, (I)] has been studied extensively because of its important physiological endogenous role (Goldberg, 1972). A great deal of effort was devoted to the synthesis of DA analogues which overcame DA problems of oral low absorption and rapid metabolism (Ince, 1990). A second line of research focused on