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Lactonization of Olefins Mediated by Mn(OAc)3: A Sonochemical Approach.

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Abstract *- The reaction of lactonization of olefins with carboxyalkyl radicals and Mn(OAc)3 was carried out under ultrasound irradiation at low temperatures Good yields of lactones were obtained in short reaction times In sonochemical conditions, reoxidation of Mn(II) occurred, allowing the development of a lactonization procedure with a catalytic amount of Mn(III)*

In our laboratory, we are interested to study the outcome of several reactions involving single electron transfer (SET) processes under ultrasound irradiation at low temperature

It is widely accepted that SET processes are greatly favoured by ultrasound [1] We started our research on the "one step" synthesis of γ-lactones from olefins in thermal conditions,[2] promoted by $Mn(OAc)_3$ and firstly developed by Heiba and Dessau,[3a] and Bush and Finkbeiner [3b]

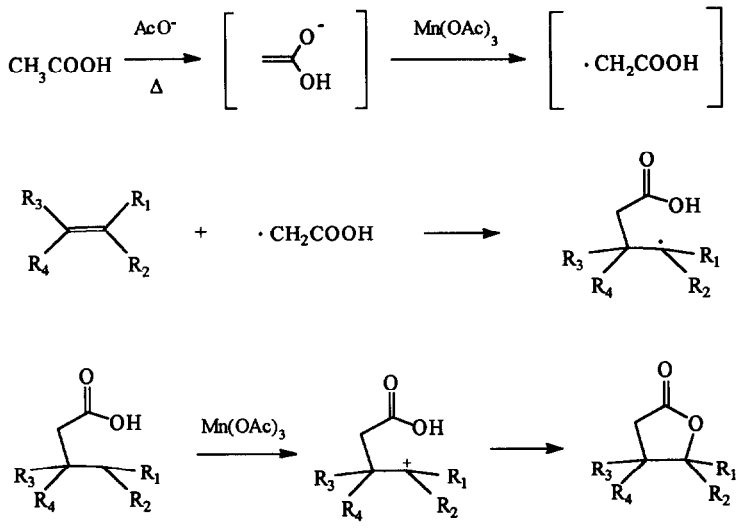
Our project was supported by several considerations The reaction mechanism, as investigated by several authors,[4] involves the selective formation and oxidation of carbon radicals by single electron transfer to transition metal oxidant species

Some consideration of the correlation between the temperature and cavitational intensity in organic solvents induced us to operate in a range of temperatures from 0°C to 10°C despite the almost complete insolubility of $Mn(OAc)_3$ in acetic acid in these conditions In fact, the maximum cavitational intensity in acetic acid is reached at 4°C

We started studying the particular reaction conditions leading in the thermal process to α-unsubstituted γ-lactones We used acetic acid as solvent and source of carboxymethyl radicals at 0°-10°C, in the presence of various olefins $Mn(OAc)_3$ and KOAc were in the same molar ratios described by Heiba and Dessau,[4] ultrasound intensities were within the range 180-300 W/cm^2

In these conditions, no reaction occurred at all and starting olefin was totally recovered after work-up A probable explanation of this unreactivity could lie in the reaction mechanism (see Scheme 1) the generation of carboxymethyl radicals could occur from the enolic (or enolate) form of acetic acid, and preliminary enolization could be strongly unfavourable at low temperatures In order to verify this hypothesis, we tried to induce the

formation of carboxymethyl radicals favouring the enolization of potassium acetate, this was done by adding basic Al_2O_3 (as enolization catalyst) to a solution of the alkene, KOAc and Mn(III) salt and sonicating the resulting mixture



Scheme 1

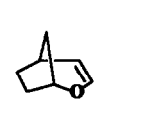
In fact, lactonic products were not obtained at all Thus, we decided to use more easily enolizable carboxylic compounds, like the monomethyl ester of malonic acid, or cyanoacetic acid in presence of KOAc, as sources of α-substituted carboxyalkyl radicals Firstly, we carried out the lactonization reaction under simple mechanical stirring at the same temperature (0-10°C) used in the sonochemical experiment, but without ultrasound irradiation In these conditions, the reaction mixture after 2-4 hours of stirring did not show any conversion of the olefin into the lactonization product

However, irradiation of the same reaction mixture at low temperature with high intensity ultrasound gave rise to complete and rapid conversion of the olefin into substituted γ-lactone

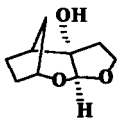
In most cases this transformation required very short times and yields were comparable or even higher than those reported in thermal methods (see Tab 1)

We tested simple olefins, like cyclohexene, and various alkenes bearing different substituents on the double bond Olefins with electron withdrawing groups were found to be rather unreactive, while very good results were obtained on enol ethers In the literature only one case of this kind of lactonization reaction of enol ethers was described, and yields reported were moderate [5] The 3-carbomethoxy-γ-lactone **12** [6] derived from 2-oxabicyclo[3 2 1]oct-3-ene **1** was particularly interesting As a matter of fact, it could be useful precursor of compounds analogous to **2** and **3** lacking the angular hydroxyl group Compounds **2** and **3** are known to be powerful antifeedants active against Egyptian cotton leaf worm (*Spodoptera littoralis*) [7] An anomalous reaction was observed for norbornene When this compound was reacted with cyanoacetic acid, the formation

of **6c** as the prevalent product was observed The formation of **6c** is caused[8] by a further reaction of initially formed **6b** with Mn(III) salt



1



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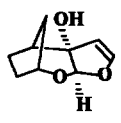

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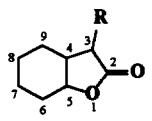
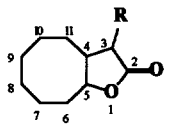
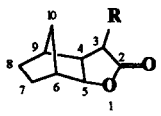


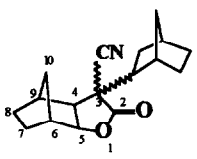
4a R = COOMe
4b R = CN



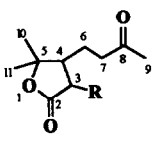
5a R = COOMe
5b R = CN



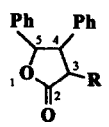
6a R = COOMe
6b R = CN



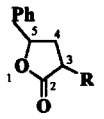
6c



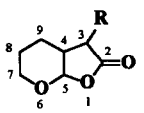
7a R = COOMe
7b R = CN



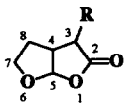
8a R = COOMe
8b R = CN



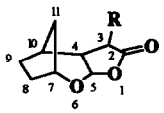
9a R = COOMe
9b R = CN



10a R = COOMe
10b R = CN



11 R = COOMe



12 R = COOMe

Sonochemical induction is particularly efficient in this reaction and this method proved to be very effective, especially for those olefins like stilbene and cyclohexene, that gave unsatisfactory results at higher temperatures using simple mechanical stirring [4,11] The behaviour of the reaction mixture under ultrasound irradiation was interesting and some important results arose from the observation of the course of the reaction

First, in "silent" conditions, the reaction mixture was initially dark brown because of the presence of $Mn(OAc)_3$ (always used in a stoichiometric amount), the dark colour tended to disappear during the reaction course and at its end the solution became colourless However, at low temperatures under sonochemical irradiation, the dark brown colour of the suspension remained unaltered even when the olefinic substrate was completely transformed into the lactonization product Although in our sonochemical experiments $Mn(OAc)_3$ was not in excess, at the end of reaction about 25% of Mn(III) salt initially added was still present (as determined by titrimetric methods)

Hence, it is probable that Mn(II) acetate formed during the reaction could be partly reoxidized to the Mn(III) salt This could be due to the formation of powerful oxidizing species, as a consequence of ultrasound irradiation effects on the solvent (e g acetic acid) It is known that sonolysis of acetic acid produces strongly

oxidizing hydroxyl radicals[9] besides other radical species and formation of H_2O_2 and CH_3CO_3H could be possible from coupling of hydroxyl radicals with themselves or with $CH_3COO\cdot$ radicals

Tab. 1 - Sonochemical Lactonization of Olefins with $Mn(OAc)_3$

Alkene	RCH_2COOH	Product	Yield (%)	Reaction time (min)
Cyclohexene	R = COOMe	**4a**	78	15
	R = CN	**4b**	65	20
Cyclooctene	R = COOMe	**5a**	70	15
	R = CN	**5b**	65	15
Norbornene	R = COOMe	**6a**	75	25
	R = CN	**6c**	50	15
6-methyl-5-hepten-2-one	R = COOMe	**7a**	75	15
	R = CN	**7b**	73	35
Trans-stilbene	R = COOMe	**8a**	71	20
	R = CN	**8b**	45	120
Styrene	R = COOMe	**9a**	62	20
	R = CN	**9b**	55	20
3,4-dihydro-2H-pyran	R = COOMe	**10a**	80	15
	R = CN	**10b**	65	20
2,3-dihydrofuran	R = COOMe	**11**	67	15
2-oxabicyclo[3 2 1]-oct-3-ene	R = COOMe	**12**	81	15

In order to verify the ability of these species to oxidize Mn(II) to Mn(III), we treated a suspension of $Mn(OAc)_2$ in acetic acid with peracetic acid or hydrogen peroxide at 0-10°C, in absence of ultrasound irradiation, under these conditions, only peracetic acid was able to oxidize Mn(II) to Mn(III)

Furthermore, the sonication for 1 hour of a corresponding mixture containing H_2O_2 and $Mn(OAc)_2$ resulted in the formation of small amounts of Mn(III) These results seemed to confirm the active role played by hydroxyl radicals in the formation of species able to oxidize Mn(II) to Mn(III)

Further confirmation of the existence of a reoxidation mechanism activated by sonochemical conditions was given by several attempts at the lactonization of 6-methyl-5-hepten-2-one, sonicating Mn(II) acetate suspensions in acetic acid, in the presence of this olefin and of several species able to produce OH· radicals under sonolysis We obtained very interesting results, that are given in Tab 2

Tab. 2 - Sonochemical Lactonization of 6-Methyl-5-hepten-2-one with $Mn(OAc)_2$ and Monomethyl Ester of Malonic Acid

Alkene	Product	Reaction conditions	Yield (%)	Reaction time (hours)
6 - Methyl - 5 - hepten - 2 - one	7a	$Mn(OAc)_2$ (2 equiv) CH_3COOH	8	2
"	"	$Mn(OAc)_2$ (2 equiv) TBHP (1 equiv)	19	2
"	"	$Mn(OAc)_2$ (2 equiv) H_2O_2 (1 equiv)	36	2
"	"	$Mn(OAc)_2$ (2 equiv) CH_3CO_3H (1 equiv)	58	2

The final evidence for a reoxidative "catalytic" mechanism was given by carrying out a sonochemical lactonization reaction on several olefins using only a catalytic amount of $Mn(OAc)_3$ (see Tab 3)

Tab. 3 - Sonochemical Lactonization of Olefins using a Catalytic Amount of $Mn(OAc)_3$

Alkene	RCH_2COOH	Product	Yield (%)	Reaction time (min)
Cyclohexene	R = COOMe	4a	22[a]	90
Cyclooctene	"	5a	39[a]	"
Norbornene	"	6a	34[a]	"
3,4 - Dihydro - 2H - Pyran	"	10a	39[b]	"
2,3 - Dihydrofuran	"	11	41[b]	"

a) These yields were obtained using 0,2 equivalents of $Mn(OAc)_3$
b) These yields were obtained using 0,1 equivalents of $Mn(OAc)_3$

These experiments gave better results with enol ethers, than with simple olefins In this way, we achieved a convenient and inexpensive procedure to lactonize olefins, that could probably be extended to other carboannulation reactions of olefins using $Mn(OAc)_3$ in acetic acid [10a,b,c]

This sonochemical method seems promising also from a stereochemical point of view As described by Fristad and Peterson,[11] lactonization of cyclohexene and cyclooctene with a potassium salt of monomethylmalonate or cyanoacetic acid in the temperature range 40-80°C leads in both cases to a mixture of cis- and trans-fused bicyclic lactones

The product mixture resulting from sonochemical lactonization of cyclohexene was less complex Using potassium monomethyl malonate we obtained only cis-fused α-carbomethoxy γ-lactones with high stereospecifity at carbon (C-3) bearing the carbomethoxy group (only one epimer was formed) On the contrary, using cyanoacetic acid on the same alkene, we obtained the expected bicyclic α-cyano γ-lactone with a cis junction, but as a mixture of epimers at carbon bearing CN group (see Experimental) These facts were evident from the comparison of nmr spectral data with those reported for the same compounds by Fristad and Peterson [11] The same behaviour was observed for 3,4-dihydro-2H-pyran with potassium monomethyl malonate, only lactonic compound **10a** was formed with high epimeric purity at C-3 A comparison of the observed $J_{4\,5}$ value (4 4 Hz) with that deduced from the dihedral angle between H-4 and H-5 (observed in Dreiding model of **10a**) suggests that also in this case a cis-fused bicyclic lactone was obtained Meanwhile, the spectral analysis of α-cyano γ-lactone **10b** showed the presence of more than one isomeric lactone Lactonization reaction carried out on cyclooctene led to the formation of cis and trans-fused lactones, either with cyanoacetic acid or monomethyl malonate **5a** showed spectral features in agreement with the presence of trans and cis-fused lactones with a 7 3 trans/cis ratio **5b** was also obtained as a mixture of isomeric lactones, but the prevalent product in the mixture was the trans-fused bicyclic lactone (trans/cis 9 1) The assignment of isomeric ratios was possible also in this case by the comparison of NMR data of these compounds with those reported in literature [11]

EXPERIMENTAL

Sonochemical reactions were carried out in a Vibracell 600 Watt probe transducer, operating between 200-300 W/cm^2 with a titanium microtip (ϕ 6,5 mm), directly connected to the horn The irradiation with ultrasond was pulsed (50% of total time) to obtain a good control of reaction temperature

2-Oxabicyclo[3 2 1]oct-3-ene **1** was prepared as described in the literature,[12] while all other alkenes were purchased from Fluka and Aldrich and used without further purification

^{1}H-NMR were recorded on a Varian XL-200 Gemini spectrometer, using TMS as internal standard in $CDCl_3$ Chemical shifts are reported in parts per million and are given in δ units, coupling constants are given in Hertz We used the following symbols to report the multiplicity and shape of signals bs (broad signal), d (doublet), dd (double doublet), dt (double triplet), m (multiplet), q (quartet), qp (quintuplet), s (singlet), se (sextet), t (triplet) ^{13}C-NMR were recorded on the same spectrometer, operating at 50 MHz ^{13}C-NMR assignments marked with * may be interchangeable The progress of reactions and chromatographic separations were monitored by TLC on silica gel plates (Merck Kieselgel 60 F_{254} ϕ 0,25 mm) Column chromatography was performed on silica gel (Merck kieselgel, 70-230 mesh)

General procedure for preparation of α-carbomethoxy-γ-lactones - To a solution of 1 3 mmol of olefin in 15 ml of glacial acetic acid, 6 3 g of the potassium salt of malonic acid monomethyl ester (40 mmol) and

700 mg of $Mn(OAc)_3\ 2H_2O$ (2 6 mmol) were added The resulting suspension was cooled in an ice-bath and irradiated with ultrasound (300 W/cm^2) under an argon atmosphere until the starting olefin disappeared (TLC) or the spot intensity remained constant in successive controls The reaction mixture was then poured into water (100 ml), and drops of a saturated solution of $Na_2S_2O_3$ were added until the solution became colourless This mixture was then extracted with Et_2O (4x50 ml), and the organic phase washed with saturated $NaHCO_3$ solution to remove acetic acid, then with brine, and finally dried over anhydrous Na_2SO_4 Removal of the solvent under reduced pressure at room temperature afforded in most cases an oily residue, which was chromatographed on silica gel column and eluted with CH_2Cl_2 to give pure α-carbomethoxy-γ-lactones

General procedure for preparation of α-cyano-γ-lactones - To a solution of 1 3 mmol of olefin in 15 ml of glacial acetic acid, 2 4 g of cyanoacetic acid (2 6 mmol), 6 g of anhydrous KOAc (61 mmol) and 700 mg of $Mn(OAc)_3\ 2H_2O$ (2 6 mmol) were added The resulting suspension was cooled in an ice-bath and irradiated with ultrasound (300 W/cm^2) under an argon atmosphere until the starting olefin disappeared (TLC) or the spot intensity remained constant in successive controls The reaction mixture was then poured into water (100 ml), then a few drops of a saturated solution of $Na_2S_2O_3$ were added until the solution became colourless

The mixture was then extracted with Et_2O (4x50 ml), the organic phase was washed with saturated $NaHCO_3$ solution to remove acetic acid, then with brine, and was finally dried over anhydrous Na_2SO_4 Removal of the solvent under reduced pressure at room temperature afforded an oily residue in most cases This residue was chromatographed on a silica gel column and eluted with CH_2Cl_2 to give pure α-cyano-γ-lactone

Compound 4a - y = 78%, Rf = 0 35 (CH_2Cl_2), cis-fused, one epimer at C-3, ^{1}H-NMR ($CDCl_3$, δ) 1 20-2 00 (8H, cm, 2H-6, 2H-7, 2H-8, 2H-9), 2 78 (1H, m, H-4), 3 29 (1H, d, J = 5 4 Hz, H-3), 3 78 (3H, s, OCH_3), 4 68 (1H, q, J_1= J_2= 5 2 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 38 85 (C-4), 47 92 (C-3), 52 98 (OCH_3), 78 25 (C-5), 167 99 (C-2), 172 25 (CO of $COOCH_3$) Anal Calcd for $C_{10}H_{14}O_4$ C 60 60, H 7 12 Found C 60 43, H 7 08

Compound 4b - y = 65%, Rf = 0 4 (CH_2Cl_2), cis-fused, epimeric mixture at C-3, ^{1}H-NMR ($CDCl_3$, δ) 1 10-2 20 (8H, cm, 2H-6, 2H-7, 2H-8, 2H-9), 2 67 (0,63H, m, H-4), 2 85 (0 27H, m, H-4), 3 46 (0 27H, d, J = 6 0 Hz, H-3), 3 86 (0 63H, d, J = 5 0 Hz, H-3), 4 56 (0 63H, bs, H-5), 4 75 (0 27H, q, J = 4 0 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 37 00 and 38 02 (C-4), 40 52 and 41 15 (C-3), 78 60 and 78 76 (C-5), 113 53 and 114 49 (CN), 168 96 (C-2) Anal Calcd for $C_9H_{11}O_2N$ C 65 43, H 6 71, N 8 48 Found C 65 22, H 6 75, N 8 35

Compound 5a y = 70%, Rf = 0 23 (CH_2Cl_2), diastereomeric mixture, ^{1}H-NMR ($CDCl_3$, δ) 1 00-2 30 (12H, m, 2H-6, 2H-7, 2H-8, 2H-9, 2H-10, 2H-11), 2 70-2 82 (1H, m, H-4), 3 24 (0 3H, d, J = 12 0 Hz, H-3), 3 28 (0 7H, d, J = 12 0 Hz, H-3), 3 78 (3H, s, OCH_3), 4 38 (1H, dt, J_1= 10 2 Hz, J_2= 4 5 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 33 14 and 34 21 (C-4), 43 11 and 44 73 (C-3), 55 39 (OCH_3), 84 16 and 84 89 (C-5), 168 36 (C-2), 170 73 (CO of COOMe) Anal Calcd for $C_{12}H_{18}O_4$ C 63 70, H 8 02 Found C 63 64, H 7 95

Compound 5b - y = 65%, Rf = 0 29 (CH_2Cl_2), diastereomeric mixture, ^{1}H-NMR ($CDCl_3$, δ) 0 90-2 20 (12H, m, 2H-6, 2H-7, 2H-8, 2H-9, 2H-10, 2H-11), 2 50-2 95 (1H, m, H-4), 3 39 (0 1H, d, J = 12 0 Hz, H-3),

3 42 (0 9H, d, J = 12 0 Hz, H-3), 4 43 (1H, dt, J_1= 9 6 Hz, J_2= 4 5 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 39 00 and 41 03 (C-4), 42 12 and 46 54 (C-3), 84 30 and 85 80 (C-5), 114 85 (CN), 167 03 (C-2) Anal Calcd for $C_{11}H_{15}O_2N$ C 68 37, H 7 82, N 7 25 Found C 68 34, H 7 71, N 7 32

Compound 6a - y = 75%, Rf = 0 33 (CH_2Cl_2), ^{1}H-NMR ($CDCl_3$, δ) 1 00-1 70 (6H, m, 2H-7, 2H-8, 2H-10), 2 18 (1H, d, J = 3 5 Hz, H-4), 2 40-2 55 (1H, m, H-9), 2 60-2 75 (1H, m, H-6), 3 20 (1H, d, J = 3 8 Hz, H-3), 3 75 (3H, s, OCH_3), 4 52 (1H, d, J = 6 7 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 40 60* (C-9), 41 39* (C-6), 46 60 (C-4), 51 73 (C-3), 53 07 (OCH_3), 85 97 (C-5), 168 79 (C-2), 172 53 (CO of COOMe) Anal Calcd for $C_{11}H_{14}O_4$ C 62 84, H 6 71 Found C 62 76, H 6 68

Compound 6c - y = 50%, Rf = 0 37 (CH_2Cl_2), diastereomeric mixture, ^{1}H-NMR ($CDCl_3$, δ) 1 00-1 90 (17H, m, 2H-7, 2H-8, 2H-10, norbornyl group), 2 16 (1H, d, J = 6 2 Hz, H-4), 2 29 (1H, bs, H-9), 2 49 (1H, bs, H-6), 4 48 (1H, t, J = 6 7 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 50 58 (C-3, assigned by APT tecniques), 84 50 and 84 85 (C-5), 116 23 (CN), 171 90 (C-2) Anal Calcd for $C_{17}H_{21}O_2N$ C 75 24, H 7 80, N 5 16 Found C 75 06, H 7 64, N 5 11

Compound 7a - y = 75%, Rf = 0 58 (CH_2Cl_2), ^{1}H-NMR ($CDCl_3$, δ) 1 23 (3H, s, 3H-10), 1 49 (3H, s, 3H-11), 1 50-1 80 (2H, m, 2H-6), 2 08 (3H, s, 3H-9), 2 41 (2H, t, J = 7 2 Hz, 2H-7), 2 52-2 70 (1H, m, H-4), 3 39 (1H, d, J = 12 6 Hz, H-3), 3 78 (3H, s, OCH_3), ^{13}C-NMR ($CDCl_3$, ppm) 20 30* (C-10), 20 47* (C-11), 22 32 (C-6), 26 82 (C-4), 29 70 (C-9), 40 95 (C-7), 48 48 (C-3), 52 98 (OCH_3), 85 93 (C-5), 169 04 (C-2), 170 57 (CO of COOMe), 207 56 (C-8) Anal Calcd $C_{12}H_{18}O_5$ C 59 50, H 7 49 Found C 59 55, H 7 44

Compound 7b - y = 73%, Rf = 0 62 (CH_2Cl_2), ^{1}H-NMR ($CDCl_3$, δ) 1 26 (3H, s, 3H-10), 1 50 (3H, s, 3H-11), 1 60-1 90 (2H, m, 2H-6), 2 18 (3H, s, 3H-9), 2 42-2 60 (1H, m, H-4), 2 71 (2H, t, J = 7 1 Hz, 2H-7), 3 54 (1H, d, J = 12 8 Hz, H-3), ^{13}C-NMR ($CDCl_3$, ppm) 19 95* (C-10), 20 15* (C-11), 21 78 (C-6), 26 82 (C-4), 29 70 (C-9), 38 12 (C-4), 40 77 (C-7), 50 63 (C-3), 87 50 (C-5), 116 12 (CN), 167 17 (C-2), 207 51 (C-8) Anal Calcd for $C_{11}H_{15}O_3N$ C 63 14, H 7 22, N 6 70 Found C 63 02, H 7 17, N 6 56

Compound 8a - y = 71%, Rf = 0 48 (CH_2Cl_2), ^{1}H-NMR ($CDCl_3$, δ) 3 76 (3H, s, OCH_3), 4 00-4 10 (2H, m, H-3, H-4), 5 38-5 50 (1H, m, H-5), 7 10-7 50 (10H, m, aromatic protons), ^{13}C-NMR ($CDCl_3$, ppm) 52 97 (OCH_3), 54 03* (C-3), 54 71* (C-4), 85 59 (C-5), 126 22-136 36 (aromatic carbons), 167 48 (C-2), 170 24 (CO of COOMe) Anal calcd for $C_{18}H_{16}O_4$ C 72 96, H 5 44 Found C 72 91, H 5 46

Compound 8b - y = 45%, Rf = 0 63 (CH_2Cl_2/Et_2O 9 1), diastereomeric mixture, ^{1}H-NMR ($CDCl_3$, δ) 3 72 (0 35H, d, J = 10 0 Hz, H-4), 3 87 (0 65H, d, J = 10 0 Hz, H-4), 4 03 (0 65 H, s, H-3), 4 09 (0 35H, s, H-3), 5 49 (1H, d, J = 10 0 Hz, H-5), 7 10-7 60 (10H, m, aromatic protons), ^{13}C-NMR ($CDCl_3$, ppm) 40 92 (C-3), 55 30 (C-4), 85 92 (C-5), 114 06 (CN), 123 35-134 54 (aromatic carbons), 166 56 (C-2) Anal Calcd for $C_{17}H_{13}O_2N$ C 77 55, H 4 97, N 5 32 Found C 77 48, H 4 93, N 5 35

Compound 9a - y = 62%, Rf = 0 56 (CH_2Cl_2/Et_2O 9 1), diastereomeric mixture, ^{1}H-NMR ($CDCl_3$, δ) 2 30-3 10 (2H, m, 2H-4), 3 65-3 80 (1H, m, H-3), 3 81 (3H, s, OCH_3), 5 41 (0 52H, dd, J_1= 10 7 Hz, J_2= 7 1 Hz, H-5), 5 70 (0 48H, t, J = 7 1 Hz, H-5), 7 20-7 51 (5H, m, aromatic protons), ^{13}C-NMR ($CDCl_3$, ppm) 34 60 and 34 73 (C-4), 47 51 and 47 61 (C-3), 53 14 (OCH_3), 79 98 and 80 47 (C-5), 120 00-138 67

(aromatic carbons), 168 16 and 168 26 (C-2), 171 61 and 171 78 (CO of COOMe) Anal Calcd for $C_{12}H_{12}O_4$ C 65 45, H 5 49 Found C 65 60, H 5 37

Compound 9b - y = 55%, Rf = 0 42 (CH_2Cl_2), diastereomeric mixture, ^{1}H-NMR ($CDCl_3$, δ) 2 20-3 22 (2H, m, 2H-4), 3 78 (0 7H, dd, J_1= 11 5 Hz, J_2= 7 6 Hz, H-3), 3 83 (0 3H, t, J = 7 6 Hz, H-3), 5 40-5 59 (1H, m, H-5), 7 20-7 50 (5H, m, aromatic protons) Anal Calcd for $C_{11}H_9O_2N$ C 70 58, H 4 84, N 7 48 Found C 70 53, H 4 71, N 7 45

Compound 10a - y = 80%, Rf = 0 39 (CH_2Cl_2/Et_2O 9 1), cis-fused, one epimer only, ^{1}H-NMR ($CDCl_3$, δ) 1 50-2 10 (4H, m, 2H-8, 2H-9), 2 70-2 90 (1H, m, H-4), 3,47 (1H, d, J = 6 9 Hz, H-3), 3 77 (3H, s, OCH_3), 3 50-4 00 (2H, m, 2H-7), 5 68 (1H, d, J = 4 4 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 20 31* (C-9), 22 72* (C-8), 37 76 (C-4), 50 68 (C-3), 53 00 (OCH_3), 63 12 (C-7), 100 01 (C-5), 167 61 (C-2), 170 25 (CO of COOMe) Anal Calcd for $C_9H_{12}O_5$ C 54 00, H 6 04 Found C 53 92, H 5 99

Compound 10b - y = 65%, Rf = 0 44 (CH_2Cl_2/Et_2O 9 1), cis-fused, epimeric mixture at C-3, ^{1}H-NMR ($CDCl_3$, δ) 1 40-2 00 (4H, m, 2H-8, 2H-9), 2 68-2 90 (1H, m, H-4), 3 50-4 10 (3H, m, 2H-7 overlapped to H-3), 5 60 (0 45H, d, J = 4 5 Hz, H-5), 5 78 (0 55H, d, J = 4 5 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 19 09*(C-9), 21 75*(C-8), 33 77 and 35 89 (C-4), 39 80 and 39 98 (C-3), 61 73 and 64 24 (C-7), 99 23 and 100 51 (C-5), 114 16 (CN), 163 53 and 167 00 (C-2) Anal Calcd for $C_8H_9O_3N$ C 57 48, H 5 42, N 8 38 Found C 57 41, H 5 37, N 8 44

Compound 11 - y = 67%, Rf = 0 41 (CH_2Cl_2/Et_2O 9 1), ^{1}H-NMR ($CDCl_3$, δ) 1 75-2 40 (2H, m, 2H-8), 3 30-3 50 (2H, m, H-3, H-4), 3 80 (3H, s, OCH_3), 3 80-4 20 (2H, m, 2H-7 partly overlapped to OCH_3), 6 17 (1H, d, J = 5 2 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 30 92 (C-8), 43 15 (C-4), 53 32 (OCH_3), 53 44 (C-3), 67 54 (C-7), 108 18 (C-5), 167 92 (C-2), 170 06 (CO of COOMe) Anal Calcd for $C_8H_{10}O_5$ C 51 61, H 5 41 Found C 51 50, H 5 39

Compound 12 - y = 81%, Rf = 0 37 (CH_2Cl_2/Et_2O 9 1), ^{1}H-NMR ($CDCl_3$, δ) 1 59-2 11 (6H, m, 2H-8, 2H-9, 2H-11), 2 49 (1H, m, H-10), 2 70-2 82 (1H, m, H-4), 3 62 (1H, d, J = 5 1 Hz, H-3), 3 79 (3H, s, OCH_3), 4 41 (1H, bs, H-7), 5 67 (1H, d, J = 10 7 Hz, H-5), ^{13}C-NMR ($CDCl_3$, ppm) 28 16*, 28 53*, 32 18* (C-8, C-9, C-11), 34 47 (C-10), 45 59 (C-4), 47 82 (C-3), 53 09 (OCH_3), 76 53 (C-7), 96 98 (C-5), 167 89 (C-2), 171 30 (CO of COOMe) Anal Calcd for $C_{11}H_{14}O_5$ C 58 40, H 6 24 Found C 58 36, H 6 17

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