Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(7):283-288

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Asymmetric synthesis and spectroscopic characterization of various *N*-substituted phthaloyl and tosyl derivatives

Ghada Lahouar[a], Ridha Touati[a*], Sonia Khamri[a], Jérôme Marrot[b] and Béchir Ben Hassine[a]

[a]*Laboratoire de Synthèse Organique Asymétrique et Catalyse Homogène (11URES56), Faculté des Sciences de Monastir, Université de Monastir, Bd. de l'Environnement, 5019 Monastir, Tunisia*
[b]*Institut Lavoisier de Versailles ILV-UMR CNRS 8180, Université de Versailles Saint-Quentin en Yvelines, 45 avenue des Etats Unis, F-78035 Versailles, France*

ABSTRACT

A convenient and efficient synthesis of series of new optically pure N-substituted α-amino esters starting from 2-methoxy-4-(2-propenyl) phenol (eugenol) and natural amino acids is described. This improved procedure offers a convenient and effective method to access some interesting molecules containing phthalimide, tosyl and alkenes functionalities.

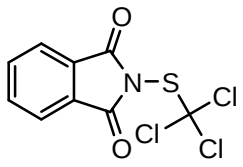
Keywords: Amino acids, phthalimide analogues, eugenol, tosyl derivatives, alkenes.

INTRODUCTION

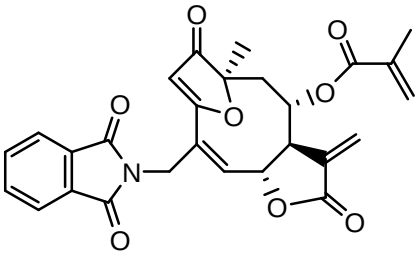
Imide group is an interesting functionality, due to its wide presence in the natural products and in the pharmacologically active compounds. The specific reactivity of imides is a result of the relative acidity of the *N* group, a direct consequence of the presence of the two carbonyl groups [1]. Phthalimide derivatives are of particular biological interest and have been reported as herbicides, insecticides, antipsychotics and anti-inflammatory agents [2]. Substituted phthalimides are used predominantly as chiral building blocks in organic synthesis and can be used as key intermediates in the preparation of bio-active compounds i.e. antibacterial analgesic, antifungal, virucidal, plant growth regulator and also in dye industry [3]. Compounds containing phthalimide moiety are distinguished by their potent fungicidal action [4-6]. The well known products namely, folpet **1**: [*N*-(trichloro methyl) thiophthalimide and compound **2** with enhanced activity against *Tripanosoma cruzi*).

On the other hand, tosyl derivatives were also found to possess biological activity [7], among them are: perindopril tosylate **3** which was indicated as substitution therapy for treatment of essential hypertension [8], cholesteryl tosylate [9] and *cis*-tosylate [10]: intermediate of ketoconazole.

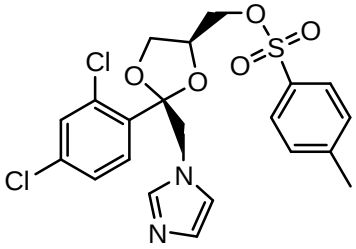
In addition to that, alkenes group is an interesting functionality and they have long intrigued organic chemists because they are motifs of many natural products such as compound **4**, [11-13] and usually served as substrates or intermediates in countless transformations. [14-16] Indeed, the synthesis of pure olefins is often a key step during the synthesis of important substances such as pheromones [17] or other natural products. [18]



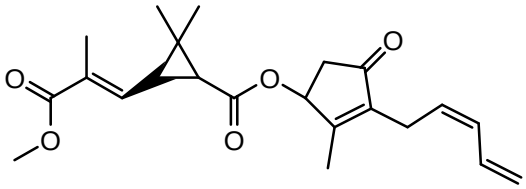
1: Folpet



2: Phthalimide derivative (Enhanced activity against Tripanosoma cruzi)



3: perindopril tosylate



4: Pyrethin II

Figure 1. Representative examples of biologically active phtalimide, tosyl and alkenes derivatives

In continuation of our research aimed toward the preparation of natural and non-natural compounds of biomedical importance [19-21] and in connection with ongoing investigations on the reactivity of natural amino acids [22-24], we inspired by the above potent pharmacological properties of these alkenes containing compounds and have been synthesized some novel *N*-substituted phthaloyl, tosyl, and alkenes derivatives.

Here in we report a synthesis and characterization of series of new optically pure *N*-substituted α-amino esters starting from 2-methoxy-4-(2-propenyl) phenol (eugenol) and natural amino acids which are of considerable interest as chiral pool agents since they are easily accessible and inexpensive enantiomerically pure compounds.

EXPERIMENTAL SECTION

Solvents are purified by standard methods. Melting points were determined on a Buchi SMP-20 capilary apparatus and are uncorrected. TLC was carried out on a Merck 60F-254 precoated silica gel plate (0.25 mm) and column chromatography was performed with Merck silica gel (70-230 mesh). NMR spectra were recorded on a Bruker AC-300 spectrometer (^{1}H NMR at 300 MHz and ^{13}C NMR at 75.5 MHz) with $CDCl_3$ as solvent and TMS as internal standard reference.

The crystal data for $C_{24}H_{25}N_1O_5$, **8c,** were recorded on a Nonis $MACH_3/CAD_4$ diffractometer.

Et_3N and $SOCl_2$ were purchased from Acros. All starting protected amino acids were prepared according to the literature procedures [22-24, 26]. In all cases, the crude protected amino acid was purified before use. Amino acids previously protected, either by phthalic anhydride or by tosyl chloride, react with thionyl chloride ($SOCl_2$) to form the corresponding acid chlorides in quantitatively yields.

Synthesis of new optically pure esters from eugenol

In a flask equipped with a condenser, the acid chloride was dissolved in anhydrous dichloromethane, under argon. Then 1 mmol of eugenol and 1.2 mmol of Et_3N were added to the solution and stirred at room temperature until complete disappearance of the starting material (TLC).

The reaction mixture was poured into a beaker containing a saturated aqueous NaCl solution. The aqueous phase was extracted with dichloromethane. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The corresponding residue was purified by column chromatography [SiO_2– cyclohexane/ethyl acetate (95:5)].

(*S*)-4-allyl-2-methoxyphenyl-2-(1,3-dioxoisoindolin-2-yl)propanoate (8a). White crystals (81% yield) **Mp** 94-96 °C [petroleum ether/ ethyl acetate (70:30)]; **$[\alpha]_D^{30}$ -16** (*c* 0.76, MeOH)**; IR(KBr) : ν cm^{-1} :** 2931, 1772, 1705 ; **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.72 (d, 3H, *J* = 7.5 Hz), 3.23 (d, 2H, *J* = 6.6 Hz), 3.66 (s, 3H), 4.93-5.00 (m, 2H), 5.16 (q, 1H , *J* = 7.2 Hz), 5.75-5.88 (m, 1H), 6.61 (d, 1H, *J* = 2.1 Hz), 6.64 (s, 1H), 6.87 (d, 1H, *J* = 8.1 Hz), 7.59-

7.63 (m, 2H), 7.72-7.78 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 15.7, 40.4, 47.8, 56.1, 113.1, 116.5, 120.9, 122.8, 123.8, 132.3, 134.6, 137.4, 138.1, 139.6, 151.1, 167.7, 168.5.

(*S*)-4-allyl-2-methoxyphenyl-3-methyl-2-(1,3-dioxoisoindolin-2-yl)butanoate (8b). White crystals (74% yield) **Mp** 84-86 °C [petroleum ether/ ethyl acetate (70:30)]; **$[\alpha]_D^{29.7}$ = -33** (*c* 0.73, MeOH)**; ^{1}H NMR** (300 MHz, $CDCl_3$): δ = 0.97 (d, 3H, *J* = 6.6 Hz), 1.20 (d, 3H, *J* = 6.6 Hz), 2.85-2.92 (m, 1H), 3.28 (d, 2H, *J* = 6.6 Hz), 3.65 (s, 3H), 4.85 (d, 1H, *J* = 8.4 Hz), 4.98-5.04 (m, 2H), 5.82-5.91 (m, 1H), 6.68 (d, 1H, *J* = 7.8 Hz), 6.70 (s, 1H), 6.94 (d, 1H, *J* = 7.8 Hz), 7.65-7.69 (m, 2H), 7.80-7.84 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 19.3, 20.8, 28.5, 40.7, 55.6, 57.5, 112.7, 116.1, 120.5, 122.5, 123.5, 131.7, 134.3, 137.0, 137.7, 139.1, 150.7, 167.0, 167.6.

(*S*)-4-allyl-2-methoxyphenyl-4-methyl-2-(1,3-dioxoisoindolin-2-yl)pentanoate (8c).White crystals (79% yield) **Mp** 82-84 °C [petroleum ether/ ethyl acetate (70:30)]; **$[\alpha]_D^{30.1}$ = -29** (*c* 0.78, MeOH)**; ^{1}H NMR** (300 MHz, $CDCl_3$): δ = 0.88 (d, 3H, *J* = 6.6 Hz), 0.91 (d, 3H, *J* = 6.6 Hz), 1.47-1.49 (m, 1H), 1.97-2.06 (m, 1H), 2.35-2.45 (m, 1H), 3.24 (d, 2H, *J* = 6.9 Hz), 3.66 (s, 3H), 4.94-5.00 (m, 2H), 5.12-5.17 (dd, 1H, *J* = 4.5 Hz, *J* = 11.4 Hz), 5.75-5.86 (m,1H), 6.61-6.64 (m, 2H), 6.86 (d, 1H, *J* = 7.8 Hz), 7.61-7.65 (m, 2H), 7.74-7.79 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 21.5, 23.6, 25.5, 37.6, 40.4, 50.9, 56.2, 113.1, 116.5, 120.9, 122.7, 123.9, 132.2, 134.6, 137.4, 138.2, 139.5, 151.1, 168.0, 168.5.

(*S*)-4-allyl-2-methoxyphenyl-3-methyl-2-(1,3-dioxoisoindolin-2-yl)pentanoate(8d). White crystals (68% yield) **Mp** 80-82 °C [petroleum ether/ ethyl acetate (70:30)]; **$[\alpha]_D^{29.5}$ = -37** (*c* 0.72, MeOH)**; ^{1}H NMR** (300MHz, $CDCl_3$): δ = 0.92 (t, 3H, *J* = 7.2 Hz), 0.99-1.18 (m, 1H), 1.21 (d, 3H, *J* = 6.6 Hz), 1.58-1.67 (m, 1H), 2.68-2.74 (m, 1H), 3.34 (d, 2H, *J* = 6,6 Hz), 3.69 (s, 3H), 4.95 (d, 1H, *J* = 8,7 Hz), 5.00-5.09 (m, 2H), 5.87-5.96 (m, 1H), 6.72-6.74 (m, 2H), 6.97 (d, 1H, *J* = 8,7 Hz), 7.73-7.76 (m, 2H), 7.87-7.91 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 10.4, 15.2, 25.1, 34.6, 39.5, 55.1, 56.4, 112.1, 115.5, 120.0, 121.9, 123.0, 131.2, 133.7, 136.5, 137.1, 138.6, 150.2, 166.6, 167.3.

(*S*)-4-allyl-2-methoxyphenyl-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate (8e). White crystals (64% yield) **Mp** 84-86 °C [petroleum ether/ ethyl acetate (70:30)]; **$[\alpha]_D^{30}$ = -45** (*c* 0.71, MeOH)**; ^{1}H NMR** (300 MHz, $CDCl_3$): δ = 3.64 (d, 2H, *J* = 6,6 Hz), 3.60-3.64 (m, 2H), 3.69 (s, 1H), 4.95-5.02 (m, 2H), 5.33-5.38 (dd, 1H, *J* = 6.3 Hz and *J* = 10.5 Hz), 5.79-5.88 (m, 1H), 6.64 (d, 1H, *J* = 1.8 Hz) 6.67 (s, 1H), 6.89-6.92 (dd, 1H, *J* = 0.9 Hz and *J* = 7.5 Hz), 7.05-7.15 (m, 5H), 7.55-7.59 (m, 2H), 7.66-7.72 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 35.1, 40.4, 53.6, 56.2, 113.1, 116.6, 121.0, 122.7, 123.8, 127.3, 129.0, 129.3, 132.0, 134.5, 137.0, 137.4, 138.1, 139.7, 151.0, 167.7, 167.8.

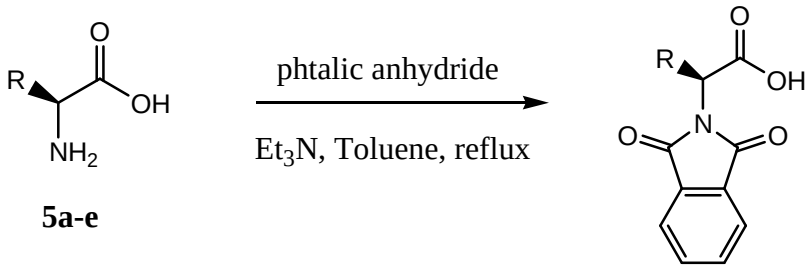
(*S*)-4-allyl-2-methoxyphenyl-2-(tosylamino)propanoate (9a). Yellow solid (67% yield) **Mp** 106-108 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.57 (d, 3H, *J* = 7.2 Hz), 2.42 (s, 3H), 3.34 (d, 2H , *J* = 6.9 Hz), 3.71 (s, 3H), 4.23-4.28 (m, 1H), 5.05-5.11 (m, 2H), 5.26 (d, 1H, *J* = 8.4 Hz), 5.87-5.96 (m; 1H), 6.61 (d, 1H, *J* = 8.1 Hz), 6.68-6.73 (m, 2H), 7.29-7.32 (m, 2H), 7.76-7.80 (m, 2H). **^{13}C NMR** (75MHz, $CDCl_3$): δ = 20.5, 21.9, 40.4, 51.9, 56.1, 113.1, 116.6, 120.9, 122.2, 127.7, 130.1, 137.2, 137.3, 137.6, 139.9, 144.0, 150.7, 171.0.

(*S*)-4-allyl-2-methoxyphenyl-3-methyl-2-(tosylamino)butanoate (9b). Yellow solid (65% yield) **Mp** 130-132 °C. **IR(KBr) : ν cm^{-1}** 3300, 1750, 1600, 1450. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 0.98 (d, 3H, *J* = 6.9Hz), 1.10 (d, 3H, *J* = 6.6Hz), 2.27-2.33 (m, 1H), 2.42 (s, 3H), 3.33 (d, 1H, *J* = 6.6 Hz), 3.69 (s, 3H), 3.99-4.04 (dd, H, *J* = 4.5 Hz and *J* = 10.2 Hz), 5.06-5.11 (m, 2H), 5.19 (d, 1H, *J* = 10.2 Hz), 5.84-5,96 (m, 1H), 6.41 (d, 1H, *J* = 8.1 Hz), 6.64-6.67 (m, 1H), 6.71 (d, 1H, *J* = 1.8 Hz), 7.25-7.31 (m, 2H), 7.74-7.78 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 17.2, 19.4, 21.8, 32.2, 40.4, 55.8, 61.2, 113.0, 116.6, 120.8, 122.3, 127.8, 130.0, 130.4, 137.2, 137.5, 139.9, 143.9, 150.8, 169.9.

(*S*)-4-allyl-2-methoxyphenyl-4-methyl-2-(tosylamino)pentanoate (9c). Yellow solid (66% yield) **Mp** 112-114 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 0.96 (d, 3H, *J* = 6Hz), 0.98 (d, 3H, *J* = 6Hz), 1.61-1.79 (m, 2H), 1.95-2.00 (m, 1H), 2.42 (s, 3H), 3.34 (d, 2H, *J* =6.6Hz), 3.71 (s, 3H), 4.15-4.23 (m, 1H), 5.06-5.11 (m, 2H), 5.17 (d, 1H, *J* = 9.9 Hz), 5.88-5.97 (m,1H), 6.46 (d, 1H, *J* = 8.1 Hz), 6.65-6.68 (dd, 1H, *J* = 1.5 Hz and *J* = 8.1 Hz), 6.71 (d, 1H, *J* = 1.5 Hz), 7.29 (d, 2H, *J* = 8.4Hz), 7.78 (d, 2H, *J*= 8.1Hz). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 21.5, 21.5, 22.9, 24.3, 40.0, 42.6, 54.5, 55.7, 112.7, 116.3, 120.5, 121.9, 127.5, 129.7, 136.8, 137.2, 139.4, 143.6, 150.5, 170.6.

RESULTS AND DISCUSSION

The α *N*-Phtalimido amino acids (Compound 6a-e) were prepared by allowing phthalic anhydride to react with a number of commercially available amino acids in refluxing nonpolar solvents such as toluene in the presence of triethylamine and separating the formed water (scheme1).

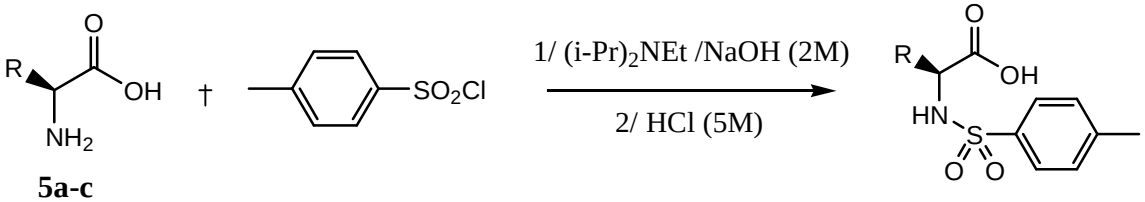


5a-e **6a-e**

a: R= CH_3; b: R= $(CH_3)_2CH$; c: R= $(CH_3)_2CHCH_2$
d:R= $CH_3CH_2CH(CH_3)$; e: R= CH_2Ph

Scheme 1

On the other hand, tosylation of α–amino acids with tosyl chloride, in a two-phase mixture of i-$PrNEt_2$ in acetone and aqueous NaOH, leads to the *N*-tosyl amino acids **7a-c** as illustrated in scheme 2,



5a-c **7a-c**

a: R= CH_3; b: R= $(CH_3)_2CH$; c: R= $(CH_3)_2CHCH_2$

Scheme 2

The treatment of **6a-e** with thionyl chloride followed by treatment with eugenol in anhydrous dichloromethane in the presence of Et_3N at 0°C to room temperature, provide the corresponding *N*-substituted phthaloyl derivatives **8a-e** with good to excellent yields (Table 2) in two steps.

The resulting products were obtained in excellent yields, and interestingly, the stereogenic center did not undergo any racemization. A single crystal X-ray crystal structure19 was obtained for (*S*)-4-allyl-2-methoxyphenyl-4-methyl-2-(1,3-dioxoisoindolin-2-yl) pentanoate (**4c**) (Figure 2).

The details of the structure refinement, is given in Table 1.

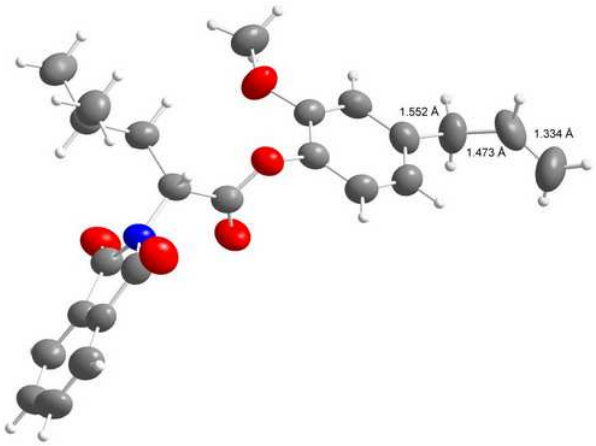
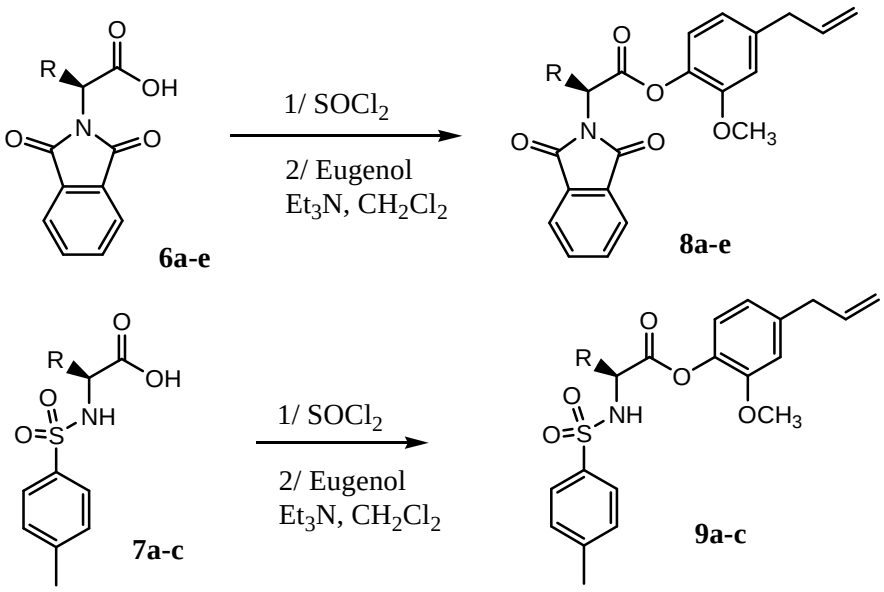


Figure 2. X-ORTEP representation of (*S*)-4-allyl-2-methoxyphenyl-4-methyl-2-(1,3-dioxoisoindolin-2-yl) pentanoate (8c). Thermal ellipsoids are drawn at enclose 50% probability [25]

The same procedure has been employed by to prepare *N*-substituted tosyl derivatives from *N*-tosyl amino acids **7a-c** and eugenol.



a: R= CH_3; b: R= $(CH_3)_2CH$; c: R= $(CH_3)_2CHCH_2$
d:R= $CH_3CH_2CH(CH_3)$; e: R= CH_2Ph

Scheme 3

In Table 2, are given the chemical yields and the physical properties of compounds **8a-e**, which have not been reported to date, As far as we know, compounds **9a-c** were also prepared for the first time during this study.

Table 1. Crystal data, parameters of data collection, and details of the refinement of the $C_{24}H_{25}NO_5$ structure

Formula / formula weight (g/mol)	$C_{24}H_{25}NO_5$ / 407.45
Crystal system	Triclinic
Space group	P1
Z	2
Lattice parameters	*a* = 5.755 (2) Å ; α = 88.377(2) ° *b* = 10.650(4) Å ; β = 81.14(2) ° *c* = 17.731(7) Å ; γ = 89.991(19) °
Volume	1073.4 (7) $Å^3$
Calculated density (g/cm^3)	1.261
Absorption coefficient, μ (mm^{-1})	0.088
F_{000}	432
Crystal size (mm^3) / colour	0.04 × 0.06 × 0.22 / colorless
Diffractometer	Bruker APEX-II CCD
Monochromator	graphite
Wavelength [K_α(Mo)]	λ = 0.71073 Å
Temperature	297 (2) K
Theta range	1.91°/ 25 °
H, k, l range	−6/6, -10/12, -21/20
Numbe of measured reflexions	16035
Number of independent reflexions	3772 [R_{int} = 0,025]
Unique reflexion included ($I > 2\sigma(I)$)	3422
Number of refined parametrs	601
Goodness-of-fit on F^2	1.05
Absorption correction	Multi-Scan
T_{min}, T_{max}	0.981, 0.997
R, Rw [$F^2 > 2\sigma(F^2)$]	0.029, 0.075
Weights	$w = 1/[\sigma^2(Fo^2) + (0{,}0249P)^2 + 7{,}2303P]$ where $P= (Fo^2+2Fc^2)/3$
Largest shift/error	0.002

Table 2. Preparation of the phthaloyl and tosyl derivatives

Entry	R	Product	Yield (%)[a]
1	CH_3	**8a**	81%
2	$(CH_3)_2CH$	**8b**	74%
3	$(CH_3)_2CHCH_2$	**8c**	79%
4	$CH_3CH_2CH(CH_3)$	**8d**	68%
5	CH_2Ph	**8e**	64%
6	CH_3	**9a**	67%
7	$(CH_3)_2CH$	**9b**	65%
8	$(CH_3)_2CHCH_2$	**9c**	66%

[a]*: In 2 steps*

CONCLUSION

In summary, we have developed a short (three steps) and efficient (average yields 64% to 81%) route to novel enantiomerically pure *N*-substituted phthaloyl and tosyl derivatives. Moreover, since the starting materials can be obtained from a variety of inexpensive enantiomerically pure amino acids and natural eugenol the present procedure is very mild for a wide variety of these compounds, and is therefore particularly well suited for the optimization of the pharmacological properties of these compounds. Ongoing work in our laboratory is currently centered on the study of these biologically interesting compounds.

REFERENCES

[1] Y. Hanbiao, T. Robert, A. Nidhi, N. Dov, *Bioorganic and Medicinal Chemistry Letter*, **2010**, 20, 4614- 4619.
[2] J. Gilvaldo, C. Vladimir, H. Gomes, G. C. Mauricio, *Molecules*, **2000**, 5, 908-915.
[3] T. W. Green, P. G. Mats, *Wiley-Interscience*, New York, **1999**, 564-566, 740-743.
[4] G. S. Gruzdyes, V. A. Zinchenko, R. I. Slovtsov, *Moscow*, **1983,** 272.
[5] Y. L. Nene, P. N. Thapliyal, *Fungicides in plant Diease Controll*, 3rd Ed., Oxford & IBH Publishing Co. *Pvt. Ltd.*, New Delhi, **1993,**170.
[6] U. S. Sree Ramulu, *Chemistry of Insecticides & Fungicides*, 2nd Ed., Oxford & IBH Publishing Co. *Pvt. Ltd*.,New Delhi, **1995**, 246.
[7] Y. Kacem, J. Kraiem, E. Kerkeni, A. Bouraoui, B. Ben Hassine, *Eur. J. Pharm. Sci*., **2002**, 16, 221.
[8] T. Kaleemullah, M. Ahmed, H. K. Sharma, *J. Chem. Pharm. Res.*, **2012**, 4, 483-490.
[9] H. S. Kim, S. H. Oh, D. Kim, I. C. Kim, K. H. Cho, Y. B. Park, *Bioorganic & Medicinal chemistry*, **1995**, 3, 367-374.
[10] B. Morgan, D. R. Dodds, A. Zaks, D. R. Andrews, R. Klesse, *J. Org. Chem.* **1997,** 62, 7736-7743.
[11] N. Matsuo, T. Takagki, K. Watanabe, N. Ohno, *Biosci. Biotechnol. Biochem*.
1993, 57, 693–694.
[12] A. J. Weinheimer, R. L. Spraggins, *Tetrahedron Lett.* **1969**, 10, 5185–5188.
[13] H. Kigoshi, Y. Shizuri, H. Niwa, K. Yamada, *Tetrahedron Lett.* **1981**, 22, 4729-4732.
[14] Y. S. Vikhe, S. M. Hande, N. Kawai, J. Uenishi, *J. Org. Chem.* **2009**, 74, 5174-
5180.
[15] M. B. Bertrand, J. D. Neukom, J. P. Wolfe, *J. Org. Chem*. **2008**, 73, 8852–8860.
[16] S. Kawamura, R. Takeuchi, A. Masuyama, M. Nojima, K. J. McCullough, *J. Org. Chem*. **1998**, 63, 5617–5622.
[17] K. Moil, *The Synthesis of Insect Pheromones. In The Total Synthesis of Natural Products;* ApSimon, J., Ed.; *Wiley Interscience*: New York, **1981**, 4, 1.
[18] J. Ackroyd, F. Scheinmann, *Chem. Soc. Rev.* **1982**, 11, 321.
[19] V. Ratovelomanana-Vidal, C. Girard, R. Touati, J. Tranchier, B. Ben Hassine, J.-P Genêt. *Advanced Synthesis & Catalysis*, **2003**, 345, 261.
[20] C. Mordant, C. Cano de Andrade, R. Touati, V. Ratovelomanana-Vidal, B. Ben Hassine, J.-P. Genêt, *Synthesis*, **2003**, 2405.
[21] R. Touati, V. Ratovelomanana-Vidal, B. Ben Hassine, J.-P Genêt, *Tetrahedron: Asymmetry*, **2006**, 17, 3400.
[22] A. Ould Aliyenne, J. Kraiıem, Y. Kacem, B. Ben Hassine, *C. R. Chimie*, **2007**, 10, 251-258
[23] N. Tka, J. Kraiıem, Y. Kacem, A. Hajri, B. Ben Hassine, *C. R. Chimie*, **2009**, 12, 1066e1071.
[24] Y. Kacem, A. Bouraouib, V. Ratovelomanana-Vidalc, J-P. Genêt, B. Ben Hassine, *C. R. Chimie*, **2002**, 5, 611–621
[25]CCDC 981250 contains crystallographic data for (*S*)-4-allyl-2-methoxyphenyl-4-methyl-2-(1,3-dioxoisoindolin-2-yl)pentanoate (4c). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44 1223336033;e-mail:deposit@ccdc.cam.ac.uk, http://www.ccdc.cam.ac.uk). The molecular formula = $C_{24}H_{25}N_1O_5$, belongs to a triclinic system, space group= P-1, parameters of the unit cell are: a=5.755(2) A˚, b=10.650(4) A˚, c=17.731(7) A˚, V=1073.4(7) A˚^{3}, D_c=1.261 mg/m^3, Z=2.
[26] A. Essersi, R. Touati, B. Ben Hassine, *Lett. Org. Chem.* **2010**, **7**, 69-72.