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Bismuth(III) Triflate-Based Catalytic Direct Opening of Oleanolic Hydroxy-γ-lactones to Afford 12-Oxo-28-carboxylic Acids

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Abstract: The bismuth(III) triflate-based catalytic direct opening of oleanolic hydroxy-γ-lactones affords the corresponding 12-oxo-28-carboxylic acid derivatives, in both acetonitrile and dichloromethane, at reflux, in high yields. Participation of an *in situ* generated Brønsted acid species from bismuth(III) triflate is most likely involved in the reaction mechanism. Full structural elucidation of the products obtained has been performed by 1D and 2D NMR techniques.

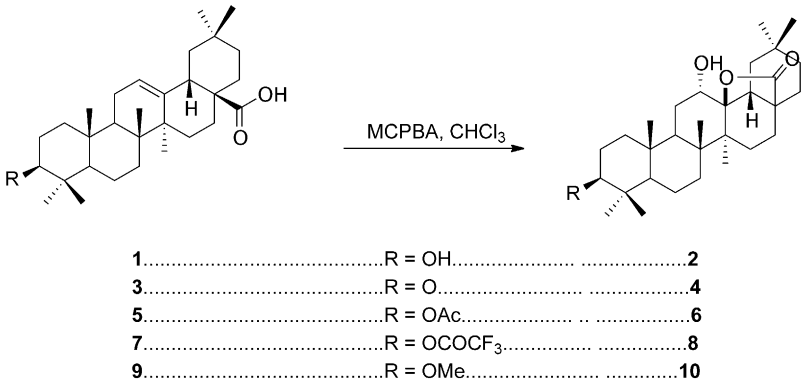
Keywords: bismuth(III) triflate; hydroxylactones; oleanolic compounds; 12-oxo-28-carboxylic acids; pentacyclic triterpenoids

Natural products have been indispensable tools for understanding the logic of biosynthesis and as platforms for developing front-line drugs.[1] It is no doubt noteworthy that some of the most interesting natural products currently available come from readily accessible natural sources such as marine organisms and plants. As the largest class of natural products, terpenoids have a variety of roles in mediating antagonist and beneficial interactions among organisms.[2] Triterpenoids have been studied for their anti-inflammatory, hepatoprotective, analgesic, antimicrobial, antimycotic, virostatic, immunomodulatory, and tonic effects. They are used in the prevention and treatment of hepatitis and above all for their cytostatic effects.[3] Oleanane triterpenoids comprise a large group of pentacyclic triterpenoids present in nature that include oleanolic acid **1** (Scheme 1), maslinic, morolic and moronic acids among others. Oleanolic acid (OA) **1** has attracted a growing interest in the last couple of decades due to its pharmacological effects, combined with its low toxicity.[4] In addition, OA **1** and its derivatives have demonstrated antibacterial,[5,6] antiparasitic,[7] antiosteoporotic,[8] antifertillity,[9] antihypertensive and antihyperlipidemic,[10] diuretic,[11] antidiabetic,[12,13] immunomodulatory,[14] anti-inflammatory,[15] antinociceptive,[16] gastroprotective,[17] hepatoprotective,[18] and anti-HIV activities,[19] as well as having the ability to inhibit the complement pathway.[20]

In the past few years, bismuth(III) salts[21,22] have emerged as convenient reagents for the development of new chemical processes[23] under more "ecofriendly" reaction conditions, which avoid the use of large amounts of toxic and corrosive materials. Indeed, it is becoming more and more common to find bismuth(III) salts-based processes for the synthesis of compounds of pharmaceutical interest.[24] As part of our ongoing work on exploiting bismuth-based processes in natural products chemistry,[25] we herein report the bismuth(III) triflate-based catalytic direct opening of oleanolic hydroxy-γ-lactones to afford the corresponding 12-oxo-28-carboxylic acid derivatives, in high yields. This novel reaction greatly simplifies the preparation of oleanolic 12-oxo-28-carboxylic acid derivatives which will allow further modifications of the oleanoic acid core.

The synthesis of the oleanolic hydroxy-γ-lactones **2**,[13] **4**,[26] **6**,[6] **8** and **10** has been accomplished using *m*-chloroperoxybenzoic acid (MCPBA)[27] (Scheme 1).

The reaction of the hydroxy-γ-lactone **2** with 1 mol% of Bi(III) triflate, in dichloromethane, at



1.....R = OH.....2
3.....R = O.....4
5.....R = OAc.....6
7.....R = $OCOCF_3$.....8
9.....R = OMe.....10

Scheme 1. Synthesis of the oleanolic hydroxy-γ-lactones **2**, **4**, **6**, **8** and **10**.

reflux, was found to afford the corresponding 12-oxo-28-carboxylic acid **11**, in 91% crude yield, after 4 h (Table 1, Scheme 2). Screening assays for solvent choice using compound **2** as substrate are depicted in Table 1. Thus, the reaction was also found to occur in acetonitrile in the same time, at reflux, quantitatively (Table 1, entry 2). However, no reaction was found to occur in ethyl acetate and only 18% product was identified in the reaction crude after 4 h, at 40 °C, using 1,4-dioxane (Table 1, entries 3 and 4).

Table 1. Opening of the oleanolic hydroxy-γ-lactone **2** with $Bi(OTf)_3 \cdot x H_2O$[a] to afford compound **11**, in different solvents.[b]

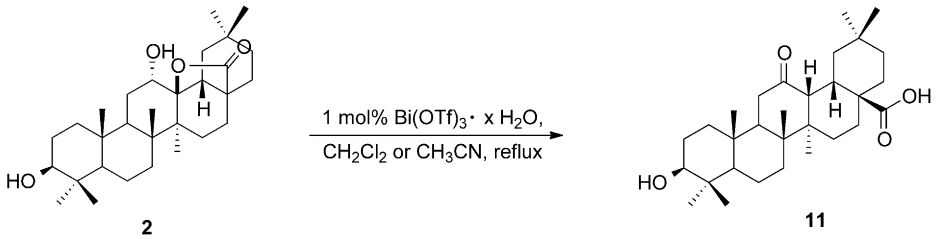
Entry	Solvent	Temp.	Time [h]	Yield [%][c]
1	CH_2Cl_2	reflux	4	91
2	CH_3CN	reflux	4	87
3	ethyl acetate	40 °C	4	–
4	1,4-dioxane	40 °C	4	18[d]

[a] Calculations based on anhydrous salt.
[b] *Reaction conditions:* 0.11 mmol of **2**, 1 mol% of $Bi(OTf)_3 \cdot x H_2O$, 1.5 mL of solvent, reflux.
[c] Isolated yield.
[d] The yield was determined by integration of the 13β-H signal in the ^1H NMR spectrum of the crude mixture.

We then moved on to establish whether other bismuth catalysts could perform the same transformation. Almost no reaction was found to occur using 1 mol% of bismuth bromide (Table 2, entry 1) or 5 mol% of bismuth chloride, in dichloromethane (entry 5). A loading amount of 10 mol% of these catalysts was needed to obtain full conversion in dichloromethane (entries 3 and 6).

Among the other metal triflates screened for this reaction, we found that 10 mol% of lanthanum triflate could complete the reaction in refluxing acetonitrile (entry 11), whereas ytterbium triflate completed the reaction at 5 mol%, in 5 h, in refluxing dichloromethane (entry 13) and at 10 mol% in refluxing acetonitrile (entry 15). Copper triflate afforded 71% of reaction product after 2 h in refluxing dichloromethane, at 1 mol% (entry 16). The reaction was found to be complete in both solvents tested using 5 mol% of this catalyst (entries 17 and 18). Despite the good results obtained with copper triflate, we chose bismuth(III) triflate as the optimal catalyst for this study based not only on the short reaction times and high substrate conversions but also on its properties as an environmentally friendly, inexpensive and easily available reagent.

The protons which result from the hydrolysis of bismuth(III) salts have been known to be the true catalytic species involved in some of the reactions in which these reagents participate.[28,29] We set out to determine the nature of the catalysis promoted by bismuth(III) triflate in the obtention of the oleanolic 12-oxo-28-carboxylic acid **11** from the hydroxy-γ-lac-



2 11

Scheme 2. Opening of the hydroxy-γ-lactone **2** with $Bi(OTf)_3 \cdot x H_2O$ to afford the 12-oxo-28-carboxylic acid **11**.

Table 2. Catalyst screening for the opening of the oleanolic hydroxy-γ-lactone **2**.[a]

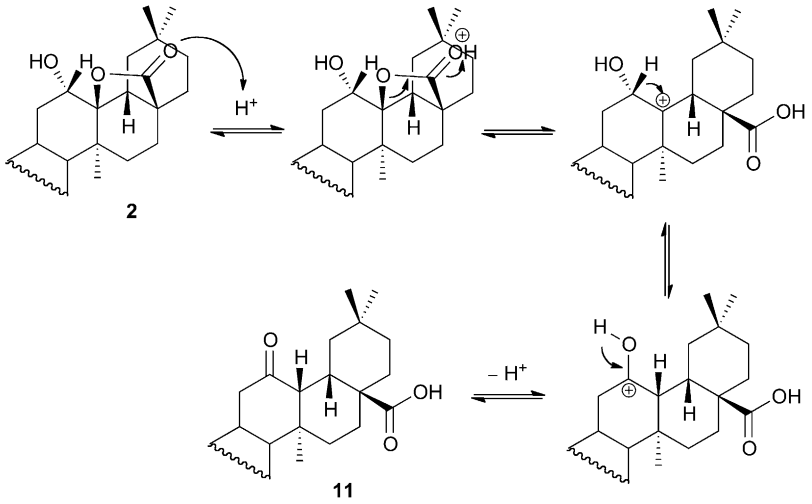
Entry	Catalyst (mol%)	Solvent	Time [h]	Yield [%][b]
1	$BiBr_3$ (1)	CH_2Cl_2	5	–
2	$BiBr_3$ (5)	CH_2Cl_2	5	29[c]
3	$BiBr_3$ (10)	CH_2Cl_2	4	98
4	$BiBr_3$ (10)	CH_3CN	8	50[c]
5	$BiCl_3$ (5)	CH_2Cl_2	5	20[c]
6	$BiCl_3$ (10)	CH_2Cl_2	5	96
7	$BiCl_3$ (10)	CH_3CN	22	66[c]
8	$La(OTf)_3$ (1)	CH_2Cl_2	5	traces
9	$La(OTf)_3$ (5)	CH_2Cl_2	5	30[c]
10	$La(OTf)_3$ (10)	CH_2Cl_2	5	38[c]
11	$La(OTf)_3$ (10)	CH_3CN	2	92
12	$Yb(OTf)_3$ (1)	CH_2Cl_2	5	62[c]
13	$Yb(OTf)_3$ (5)	CH_2Cl_2	5	97
14	$Yb(OTf)_3$ (10)	CH_2Cl_2	4	95
15	$Yb(OTf)_3$ (10)	CH_3CN	2	94
16	$Cu(OTf)_2$ (1)	CH_2Cl_2	2	71[c]
17	$Cu(OTf)_2$ (5)	CH_2Cl_2	4	94
18	$Cu(OTf)_2$ (5)	CH_3CN	2	92
19	$Bi(OTf)_3{\cdot}x\,H_2O$ (1)[d]	CH_3CN	4	96
20	$Bi(OTf)_3{\cdot}x\,H_2O$ (1)[d]	CH_2Cl_2	4	93

[a] *Reaction conditions:* 0.16 mmol of **2**, 2 mL of solvent, reflux.
[b] Isolated yield.
[c] The yield was determined by integration of the 13β-H signal on the ^1H NMR spectrum of the crude mixture.
[d] Calculations based on anhydrous salt.

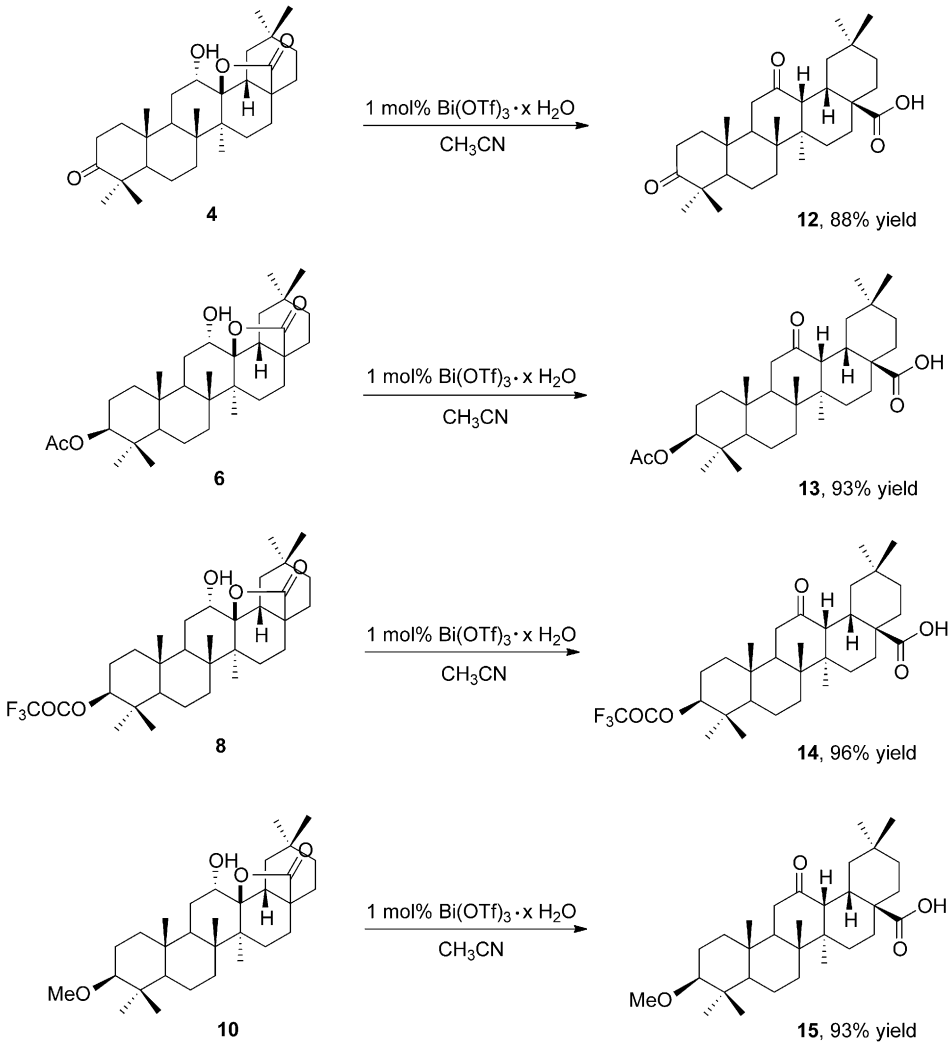
tone **2** (Scheme 2). When the reaction was performed in the presence of a well-known proton scavenger, 2,6-di-*tert*-butylpyridine, which binds to protons only and is unable to coordinate to metal ions due to the bulky *tert*-butyl groups[29] [0.11 mmol of **2**, 1 mol% $Bi(OTf)_3{\cdot}x\,H_2O$, 10 mol% scavenger, 1.5 mL CH_2Cl_2, reflux, 4 h], no reaction was found to occur. Again no reaction was found to occur in the presence of 10 mol% of $BiPh_3$ [0.11 mmol of **2**, 1 mol% $Bi(OTf)_3{\cdot}x\,H_2O$, 1.5 mL CH_2Cl_2, reflux, 4 h], another proton scavenger due to the high lability of the Bi–Ph bond under acidic conditions.[22] In sharp contrast, full conversion was achieved in the presence of 10 mol% TfOH (0.11 mmol of **2**, 1.5 mL CH_2Cl_2, reflux, 4 h), indicating that bismuth(III) triflate is hydrolyzed under these reaction conditions to afford a Brønsted acid species *in situ* which acts as the true catalyst. This species could promote ring opening of the 13β,28-olide group by creating a tertiary carbocation at C-13 which induces stereoselective 1,2-migration of the 12β-H to the 13β-position. In fact, as pointed out by Kočovský et al., non-concerted Wagner–Meerwein-type rearrangements with development of carbocation centres, result in 1,2-migration that occurs on the same plane (sp^2 alignment factor).[30] Thus, a plausible reaction mechanism is formation of a carbocation centred at C-12 due to the 12β-H→13β-H shift with rearrangement of the 12α-hydroxy group to afford the corresponding 12-oxo-28-carboxylic acid **11** (Scheme 3).

We extended this new bismuth(III) triflate-based process to other oleanolic hydroxy-γ-lactones under optimized reaction conditions (Scheme 4). Acetonitrile was chosen over dichloromethane to avoid manipulation of halogenated solvents. Thus, the oleanolic hydroxy-γ-lactones **4**, **6**, **8**, and **10** were fully converted to the respective 12-oxo-28-carboxylic acids **12**–**15**, in very high yields.

The acetoxy and trifluoroacetoxy groups of compounds **6** and **8** remained unchanged using the optimized reaction conditions. Structural elucidation of the oleanolic 12-oxo-28-carboxylic acids **11**–**15** obtained was performed by 1D and 2D NMR techniques. The proton signal for 13-H was assigned based on the HMBC correlation that it displayed with the



Scheme 3. Suggested mechanism for the opening of the hydroxy-γ-lactone **2**.



Scheme 4. Opening of the hydroxy-γ-lactones **4**, **6**, **8** and **10** with $Bi(OTf)_3 \cdot x\,H_2O$ to afford the 12-oxo-28-carboxylic acids **12**–**15**.

signal at 211.7 ppm belonging to the carbonyl group at C-12, for compound **11**. The correlation between the 18β-H signal at 2.75 ppm and the 13-H signal at 2.67 ppm on the COSY spectrum together with the existence of a NOESY correlation between these two signals is consistent with a 13β-H stereochemistry. The same pattern was found for compounds **12**–**15** on the respective 2D NMR spectra.

In conclusion, we have found that catalytic amounts of bismuth(III) triflate catalyze the direct opening of oleanolic hydroxy-γ-lactones to afford the corresponding 12-oxo-28-carboxylic acid derivatives in acetonitrile or dichloromethane, at reflux, in high yields. This novel reaction is most likely to proceed *via* an *in situ* generated Brønsted acid species from bismuth(III) triflate which works as the true catalyst, and further illustrates the use of the environmentally friendly, inexpensive, and easily obtainable bismuth salts in organic chemistry. To the best of our knowledge, compounds **7**, **8**, **10**, **14**, and **15** are new.

Experimental Section

General Procedure for the Conversion of Oleanolic Hydroxy-γ-lactones into the Corresponding 12-Oxo-28-carboxylic Acid Derivatives

3β-Hydroxy-12-oxoolean-28-oic acid (11): Compound **2** (75 mg, 0.16 mmol) and bismuth(III) triflate (Sigma–Aldrich, Co) (1.05 mg, 0.0016 mmol) were placed in acetonitrile (2 mL), under magnetic stirring, at reflux, for 4 h. The mixture was then concentrated under reduced pressure. Ethyl acetate (20 mL) and water (10 mL) were added and the aqueous phase was further extracted with ethyl acetate (2×30 mL). The organic phase was washed with 10% aqueous $NaHCO_3$ solution (2×20 mL), water (20 mL) and brine (20 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give compound **11**[31] as a white solid; yield: 72 mg (96%); mp 302–304 °C. IR: ν = 3500, 1693 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 0.77$ (s, 3H), 0.85 (s, 3H), 0.90 (s, 3H), 0.94 (s, 3H), 0.97 (s, 3H), 0.98 (s, 6H), 2.67 (d, 1H, $J = 4.1$ Hz, 13β-H), 2.75 (m, 1H,

18β-H), 3.20 (m, 1H, 3α-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 15.2, 15.3, 16.4, 18.2, 20.5, 22.5, 23.1, 27, 27.5, 27.9, 30.6, 31.8, 31.8, 33, 33.3, 34.4, 36.1, 36.9, 37.9, 38.5, 38.8, 41.2, 41.9, 47.2, 49.7, 51.8, 55, 78.6 (C-3), 183.9 (C-28), 211.7 (C-12); EI-MS: *m*/*z* (%) = 473 (2) M+1; 411 (59); 263 (47); 217 (100); 206 (82); 189 (71); 177 (61); 104 (41).

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References

[1] J. Clardy, C. Walsh, *Nature* **2004**, *432*, 829–837.
[2] J. Gershenzon, N. Dudareva, *Nature Chem. Biol.* **2007**, *3*, 408–414.
[3] a) M. B. Sporn, K. T. Liby, M. M. Yore, L. Fu, J. M. Lopchuk, G. W. Gribble, *J. Nat. Prod.* **2011**, *74*, 537–545; b) P. Dzubak, M. Hajduch, D. Vydra, A. Hustova, M. Kvasnica, D. Biedermann, L. Markova, M. Urban, J. Sarek, *Nat. Prod. Rep.* **2006**, *23*, 394–411.
[4] J. A. R. Salvador, A. S. Leal, R. C. Santos, in: *Pentacyclic Triterpenes as Promising Agents in Cancer*, (Ed.: J. A. R. Salvador), Nova Science Publishers, **2010**, ISBN: 978-1-60876-973-5.
[5] a) S. Fontanay, M. Grare, J. Mayer, C. Finance, R. E. Duval, *J. Ethnopharmacol.* **2008**, *120*, 272–276; b) T. Tanachatchairatana, J. B. Bremner, R. Chokchaisiri, A. Suksamrarn, *Chem. Pharm. Bull.* **2008**, *56*, 194–198; c) J. F. Rivero-Cruz, M. Zhu, A. D. Kinghorn, C. D. Wu, *Phytochem. Lett.* **2008**, *1*, 151–154; d) K. Horiuchi, S. Shiota, T. Hatano, T. Yoshida, T. Kuroda, T. Tsuchiya, *Biol. Pharm. Bull.* **2007**, *30*, 1147–1149; e) J. Q. Gu, Y. H. Wang, S. G. Franzblau, G. Montenegro, B. N. Timmermann, *Z. Naturforsh. C* **2004**, *59*, 797–802.
[6] F. Hichri, H. Ben Jannet, J. Cheriaa, S. Jegham, Z. Mighri, *Compt. Rend. Chim.* **2003**, *6*, 473–483.
[7] a) S. C. B. Gnoatto, L. Dalla Vechia, C. L. Lencina, A. Dassonville-Klimpt, S. Da Nascimento, D. Mossalayi, J. Guillon, G. Gosmann, P. Sonnet, *J. Enzyme Inhib. Med. Chem.* **2008**, *23*, 604–610; b) E. C. Torres-Santos, D. Lopes, R. R. Oliveira, J. P. P. Carauta, C. A. B. Falcao, A. A. C. Kaplan, B. Rossi-Bergmann, *Phytomedicine* **2004**, *11*, 114–120.
[8] Y. Zhang, J. X. Li, J. W. Zhao, S. Z. Wang, Y. Pan, K. Tanaka, S. Kadota, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1629–1632.
[9] M. Rajasekaran, J. S. Bapna, S. Lakshmanan, A. G. R. Nair, A. J. Veliath, M. Panchanadam, *J. Ethnopharmacol.* **1988**, *24*, 115–121.
[10] a) L. I. Somova, F. O. Shode, M. Mipando, *Phytomedicine* **2004**, *11*, 121–129; b) L. O. Somova, A. Nadar, P. Rammanan, F. O. Shode, *Phytomedicine* **2003**, *10*, 115–121.
[11] M. E. Alvarez, A. O. M. Maria, J. R. Saad, *Phytother. Res.* **2002**, *16*, 71–73.
[12] a) Y. N. Zhang, W. Zhang, D. Hong, L. Shi, Q. Shen, J. Y. Li, J. Li, L. H. Hu, *Bioorg. Med. Chem.* **2008**, *16*, 8697–8705; b) X. A. Wen, H. B. Sun, J. Liu, K. G. Cheng, P. Zhang, L. Y. Zhang, J. Hao, L. Y. Zhang, P. Z. Ni, S. E. Zographos, D. D. Leonidas, K. M. Alexacou, T. Gimisis, J. M. Hayes, N. G. Oikonomakos, *J. Med. Chem.* **2008**, *51*, 3540–3554; c) J. Chen, Y. C. Gong, J. Liu, W. Y. Hua, L. Y. Zhang, H. B. Sun, *Chem. Biodiversity* **2008**, *5*, 1304–1312; d) J. Chen, J. Liu, L. Y. Zhang, G. Z. Wu, W. Y. Hua, X. M. Wu, H. B. Sun, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2915–2919.
[13] M. S. Ali, M. Jahangir, S. S. ul Hussan, M. I. Choudhary, *Phytochemistry* **2002**, *60*, 295–299.
[14] a) N. T. Dat, I. S. Lee, X. F. Cai, G. Shen, Y. H. Kim, *Biol. Pharm. Bull.* **2004**, *27*, 426–428; b) T. J. Raphael, G. Kuttan, *Phytomedicine* **2003**, *10*, 483–489.
[15] a) N. Banno, T. Akihisa, H. Tokuda, K. Yasukawa, H. Higashihara, M. Ukiya, K. Watanabe, Y. Kimura, J. Hasegawa, H. Nishino, *Biosci. Biotechnol. Biochem.* **2004**, *68*, 85–90; b) E. M. Giner-Larza, S. Manez, M. C. Recio, R. M. Giner, J. M. Prieto, M. Cerda-Nicolas, J. L. Rios, *Eur. J. Pharmacol.* **2001**, *428*, 137–143; c) T. Ringbom, L. Segura, Y. Noreen, P. Perera, L. Bohlin, *J. Nat. Prod.* **1998**, *61*, 1212–1215.
[16] a) J. L. Maia, R. C. P. Lima-Junior, C. M. Melo, J. P. David, J. M. David, A. R. Campos, F. A. Santos, V. S. N. Rao, *Pharmacol. Res.* **2006**, *54*, 282–286; b) J. L. Maia, R. C. P. Lima-Junior, J. P. David, J. M. David, F. A. Santos, V. S. Rao, *Biol. Pharm. Bull.* **2006**, *29*, 82–85.
[17] a) M. Sanchez, C. Theoduloz, G. Schmeda-Hitschmann, I. Razmilic, T. Yanez, J. A. Rodriguez, *Life Sci.* **2006**, *79*, 1349–1356; b) J. A. Rodriguez, L. Astudillo, G. Schmeda-Hirschmann, *Pharmacol. Res.* **2003**, *48*, 291–294; c) L. Astudillo, J. A. Rodriguez, G. Schmeda-Hirschmann, *J. Pharm. Pharmacol.* **2002**, *54*, 583–588.
[18] a) S. A. Reisman, L. M. Aleksunes, C. D. Klaassen, *Biochem. Pharmacol.* **2009**, *77*, 1273–1282; b) J. Liu, Q. Wu, Y. F. Lu, J. B. Pi, *Biochem. Pharmacol.* **2008**, *76*, 922–928; c) N. Y. Kim, M. K. Lee, M. J. Park, S. J. Kim, H. J. Park, J. W. Choi, S. H. Kim, S. Y. Cho, J. S. Lee, *J. Med. Food* **2005**, *8*, 177–183; d) K. A. Kim, J. S. Lee, H. J. Park, J. W. Kim, C. J. Kim, I. S. Shim, N. J. Kim, S. M. Han, S. Lim, *Life Sci.* **2004**, *74*, 2769–2779; e) T. K. Yim, W. K. Wu, W. F. Pak, K. M. Ko, *Phytother. Res.* **2001**, *15*, 589–592; f) H. G. Jeong, *Toxicol. Lett.* **1999**, *105*, 215–222; g) J. Liu, Y. P. Liu, A. Parkinson, C. D. Klaassen, *J. Pharmacol. Exp. Ther.* **1995**, *275*, 768–774; h) J. Liu, Y. P. Liu, C. D. Klaassen, *Acta Pharmacol. Sin.* **1995**, *16*, 97–102; i) Y. P. Liu, H. Kreppel, J. Liu, S. Choudhuri, C. D. Klaassen, *J. Pharmacol. Exp. Ther.* **1993**, *266*, 400–406; j) J. Liu, Y. P. Liu, C. Madhu, C. D. Klaassen, *J. Pharmacol. Exp. Ther.* **1993**, *266*, 1607–1613.
[19] a) Y. M. Zhu, J. K. Shen, H. K. Wang, L. M. Cosentino, K. H. Lee, *Bioorg. Med. Chem. Lett.* **2001**, *11*, 3115–3118; b) C. M. Ma, N. Nakamura, M. Hattori, H. Kakuda, J. C. Qiao, H. L. Yu, *J. Nat. Prod.* **2000**, *63*, 238–242; c) Y. Kashiwada, T. Nagao, A. Hashimoto, Y. Ikeshiro, H. Okabe, L. M. Cosentino, K. H. Lee, *J. Nat. Prod.* **2000**, *63*, 1619–1622; d) Y. Kashiwada, H. K. Wang, T. Nagao, S. Kitanaka, I. Yasuda, T. Fujioka, T. Yamagishi, L. M. Cosentino, M. Kozuka, K. Okabe, Y.

Ikeshiro, C. Q. Hu, E. Yeh, K. H. Lee, *J. Nat. Prod.* **1998**, *61*, 1090–1095.

[20] a) H. Assefa, A. Nimrod, L. Walker, R. Sindelar, *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1619–1623; b) H. Assefa, A. Nimrod, L. Walker, R. Sindelar, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1889–1894.

[21] a) T. Ollevier, Z. Li, *Adv. Synth. Catal.* **2009**, *351*, 3251–3259; b) R. M. Hua, *Curr. Org. Synth.* **2008**, *5*, 1–27; c) H. Gaspard-Iloughmane, C. Le Roux, in: *Acid catalysis in modern organic chemistry*, (Eds.: H. Yamamoto, K. Ishihara), John Wiley & Sons, **2008**, pp 551–588; d) H. Gaspard-Iloughmane, C. Le Roux, *Trends Org. Chem.* **2006**, *11*, 65–80; e) H. Gaspard-Iloughmane, C. Le Roux, *Eur. J. Org. Chem.* **2004**, 2517–2532; f) N. M. Leonard, L. C. Wieland, R. S. Mohan, *Tetrahedron* **2002**, *58*, 8373–8397; g) H. Suzuki, T. Ikegami, Y. Matano, *Synthesis* **1997**, 249–267.

[22] H. Suzuki, Y. Matano, *Organobismuth chemistry*, Elsevier, **2001**.

[23] a) T. Ollevier, J. E. Bouchard, V. Desyroy, *J. Org. Chem.* **2008**, *73*, 331–334; b) M. Rueping, B. J. Nachtsheim, W. Ieawsuwan, *Adv. Synth. Catal.* **2006**, *348*, 1033–1037; c) H. Sun, R. Hua, S. Chen, Y. Yin, *Adv. Synth. Catal.* **2006**, *348*, 1919–1925; d) P. W. Anzalone, A. R. Baru, E. M. Danielson, P. D. Hayes, M. P. Nguyen, A. F. Panico, R. C. Smith, R. S. Mohan, *J. Org. Chem.* **2005**, *70*, 2091–2096; e) S. Antoniotti, E. Duñach, *Eur. J. Org. Chem.* **2004**, 3459–3464; f) N. Srivastava, B. K. Banik, *J. Org. Chem.* **2003**, *68*, 2109–2114.

[24] a) J. A. R. Salvador, R. M. A. Pinto, S. M. Silvestre, *Mini Rev. Org. Chem.* **2009**, *6*, 241–274; b) J. A. R. Salvador, R. M. A. Pinto, S. M. Silvestre, *Curr. Org. Synth.* **2009**, *6*, 426–470; c) J. S. Slade, J. A. Vivelo, D. J. Parker, J. Bajwa, H. Liu, M. Girgis, D. T. Parker, J. Repic, T. Blacklock, *Org. Process Res. Dev.* **2005**, *9*, 608–620; d) P. Wipf, T. D. Hopkins, *Chem. Commun.* **2005**, 3421–3423; e) K. C. Nicolaou, G. E. A. Carenzi, V. Jeso, *Angew. Chem.* **2005**, *117*, 3963–3967; *Angew. Chem. Int. Ed.* **2005**, *44*, 3895–3899; f) P. A. Evans, J. Cui, S. J. Gharpure, A. Polosukhin, H. R. Zhang, *J. Am. Chem. Soc.* **2003**, *125*, 14702–14703; g) P. A. Evans, J. Cui, S. J. Gharpure, *Org. Lett.* **2003**, *5*, 3883–3885.

[25] a) J. A. R. Salvador, S. M. Silvestre, R. M. A. Pinto, *Molecules* **2011**, *16*, 2884–2913; b) J. A. R. Salvador, R. M. A. Pinto, R. C. Santos, C. Le Roux, A. M. Beja, J. A. Paixao, *Org. Biomol. Chem.* **2009**, *7*, 508–517; c) R. M. A. Pinto, J. A. R. Salvador, C. Le Roux, J. A. Paixao, *J. Org. Chem.* **2009**, *74*, 8488–8491; d) R. M. A. Pinto, J. A. R. Salvador, C. Le Roux, R. A. Carvalho, A. M. Beja, J. A. Paixao, *Tetrahedron* **2009**, *65*, 6169–6178; e) R. M. A. Pinto, J. A. R. Salvador, C. Le Roux, R. A. Carvalho, M. R. Silva, A. M. Beja, J. A. Paixao, *Steroids* **2008**, *73*, 549–561; f) R. M. A. Pinto, J. A. R. Salvador, C. Le Roux, *Tetrahedron* **2007**, *63*, 9221–9228; g) R. M. A. Pinto, J. A. R. Salvador, C. Le Roux, *Synlett* **2006**, 2047–2050; h) J. A. R. Salvador, S. M. Silvestre, *Tetrahedron Lett.* **2005**, *46*, 2581–2584.

[26] T. Konoike, K. Takahashi, Y. Araki, I. Horibe, *J. Org. Chem.* **1997**, *62*, 960–966.

[27] T. Konoike, Y. Araki, Y. Kanda, *Tetrahedron Lett.* **1999**, *40*, 6971–6974.

[28] a) T. Ollevier, Z. Y. Li, *Adv. Synth. Catal.* **2009**, *351*, 3251–3259; b) T. Ollevier, E. Nadeau, *Org. Biomol. Chem.* **2007**, *5*, 3126–3134; c) R. Dumeunier, I. E. Markó, *Tetrahedron Lett.* **2004**, *45*, 825–829.

[29] T. C. Wabnitz, J. Q. Yu, J. B. Spencer, *Chem. Eur. J.* **2004**, *10*, 484–493.

[30] P. Kočovský, F. Tureček, V. Langer, J. Podlahova, J. Podlaha, *J. Org. Chem.* **1986**, *51*, 4888–4891.

[31] a) D. H. R. Barton, N. J. Holness, *J. Chem. Soc.* **1952**, 78–92; b) P. Dietrich, O. Jeger, *Helv. Chim. Acta* **1950**, *33*, 711–724.

