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Titanium-catalyzed Reformatsky-type reaction

Laura Sgreccia, Marco Bandini, Stefano Morganti, Arianna Quintavalla, Achille Umani-Ronchi, Pier Giorgio Cozzi *

Dipartimento di Chimica "G. Ciamician", Università di Bologna, Via Selmi, 2 40126 Bologna, Italy

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Abstract

A catalytic titanium mediated Reformatsky reaction is presented. The technique employs cyclopentadienyltitaniumdichloride(IV) (10 mol%) in conjunction with Mn (2 equiv.), as the stoichiometric reductant, and $(CF_3CO)_2O$ (1.5 equiv.), as the scavenger, and it is based on the formation of titanocene(III) chloride as a mild and homogeneous single-electron reductant. The reaction gives moderate yields of the desired Reformatsky adduct, and it works well with aromatic and aliphatic aldehydes.

Keywords: Reformatsky reaction; Titanium; Mn; Catalysis

1. Introduction

The Reformatsky reaction [1], discovered more than 115 years ago, is still a well established method widely used in synthesis allowing the straightforward addition of zinc enolates to aldehydes, ketones, or imines through the direct insertion of zinc into α-halogenated ketones, or esters. Unfortunately, the reaction is sensitive to several reaction parameters, and in particular, quality of the zinc dust can strongly halter the performance of the processes, being the reaction initiated by insertion of zinc into the carbon–halogen bond. In this context, several attempts have been addressed toward this issue with particular concern to sources and quality of activated zinc [2].

Recently, a new type of Reformatsky reaction in which ZnR'_2 ($R'_2 = Me, Et$) was used as a zinc source and $RhCl(PPh)_3$ [3] or $Ni(PPh_3)_2Cl_2$ [4] as catalysts, were described. The new homogeneous variants of the Reformatsky reaction have been used in developing asymmetric versions, with the introduction of chiral auxiliaries [5], or ligands [6]. We have successfully developed an enantioselective catalytic version of the homogeneous Reformatsky reaction promoted by ClMn(Salen) [7], and a catalytic imino Reformatsky reaction in the presence of 20 mol% of *N*-methylephedrine [8]. Our methodologies employed the rather expensive Me_2Zn as reducing agent. Although Et_2Zn and Me_2Zn could be readily prepared [9], from a practical standpoint the employment of manganese or zinc dust as reductants in the presence of a suitable chiral metal complex will be advantageous.

Fürstner has introduced the use of Zn and Mn, in combination with a scavenger, in catalytic redox reactions [10]. A catalytic McMurry type reaction was realized by the employment of catalytic amount of titanium, in the presence of stoichiometric amount of Zn and Me_3SiCl as scavenger [10a], while the catalytic version of the Nozaki–Hiyama–Kishi–Takai reaction [10b] was described with the employment of $CrCl_3$ in catalytic amount. Both these protocols were used in the presence of chiral ligands permitting the carbon–carbon bond formation in a catalytic asymmetric fashion [11]. On the other hand, interesting Reformatsky-type reaction based on chromium were described by Wessjohann [12]. Although toxic Cr(VI) is not involved in these stoichiometric or catalytic processes, stringent environmental issue asks about the development of "greener" processes. Titanium complexes are considered environmental friendly compounds of practical use and

* Corresponding author. Tel.: +39 051 2099511; fax: +39 051 2099456.
E-mail address: piergiorgio.cozzi@unibo.it (P.G. Cozzi).

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titanium(III) complexes are active and mild reducing agents [13]. In this paper we disclose our preliminary results towards the development of a unprecedented catalytic Ti/Mn redox cycle for Reformatsky reaction with aliphatic and aromatic aldehydes.

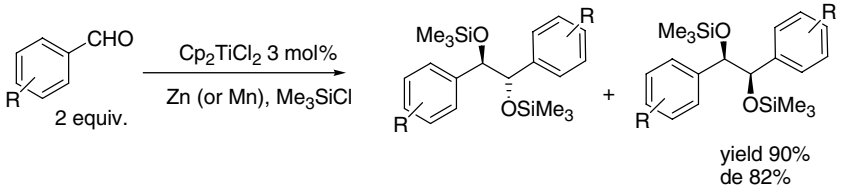
2. Result and discussion

Titanocene(III) chloride (Cp_2TiCl "Nugent's reagents") is a mild and useful reductant that was used in the single-electron opening epoxides and subsequent trapping of the resulting β-titanoxy radicals [14,15]. It found also application in the reduction of aromatic aldehydes [16], vicinal dihalides [17], sulfoxides [18], nitroarene [18], α-halo carbonyl species [19], and in living radical polymerization [20]. Based on these observations, Little recently reported a Reformatsky reaction in which stoichiometric amount of Cp_2TiCl was used [21]. This method affords high yields in the range of 88–92% with aliphatic aldehydes. Although the catalytic use of titanocene in the presence of Zn in Reformatsky reactions was reported by Ding [22], it was unclear which species (i.e. zinc or titanium (III)) was the active reductant [23]. Major drawback of the chemistry described by Little consists in the use of the stoichiometric amount of titanocene along with the limitation to aliphatic aldehydes. In fact, it is well known that aromatic aldehydes easily undergo pinacol coupling if treated with titanocene(III) in stoichiometric [24] or catalytic amount [25] (Scheme 1).

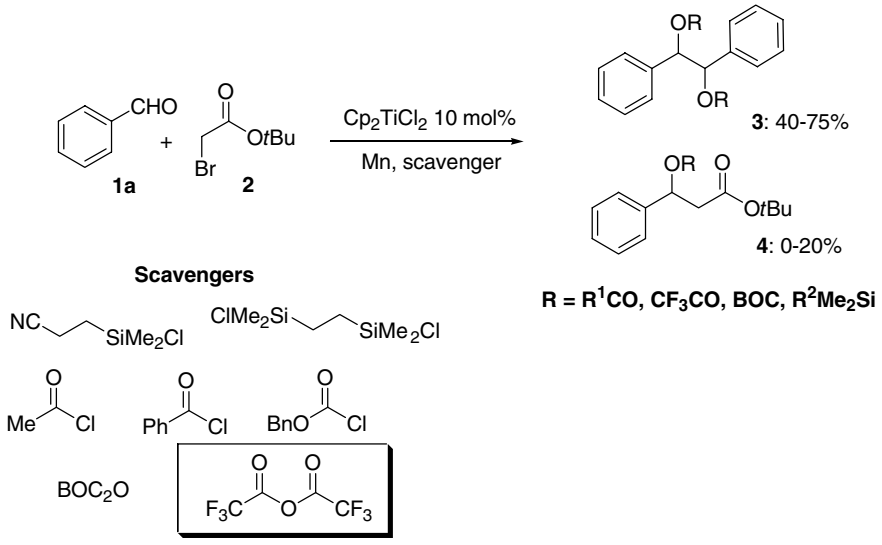
In order to study a truly catalytic titanium-mediated Reformatsky reaction, we selected benzaldehyde **1a** and *tert*butyl bromoacetate as reaction partners. The reaction was performed in CH_3CN using catalytic amount of Cp_2TiCl_2 (10 mol%) in the presence of stoichiometric amount of Mn as the reducing agent. A range of scavengers, able to cleave the oxo-titanium intermediate liberating the organic products from the titanium complex, were tested (Scheme 2). Frequently, the pinacol product **3** was isolated as the major product, while no traces of desired **4** were obtained. Quite interestingly, when the reaction was performed in the presence of trifluoroacetic anhydride as the scavenger, we were able to observe the formation of the desired adduct in modest amount.

The reaction was optimized by varying different reaction parameters, and Table 1 reports selected experiments. Among the different reaction solvents examined, CH_3CN gave the better yield, while the best catalyst was Cp_2TiCl_2. Other titanocenes were examined as well, namely $CpTiCl_3$, $Cp^*_2TiCl_2$, Cp^*TiCl_3, $Cp^{Si}_2TiCl_2$, $Cp_2Ti(OTf)_2$, $Cp^{Me}_2TiCl_2$, but they were not able to improve the yield of the reaction. The product was isolated after basic hydrolysis of the trifluoroacetate derivatives. Experiments conduced with different bromoacetates showed that *tert*butyl bromoacetate gives better yields (entry 4).

A key point of this Reformatsky reaction is the deprotection step, that is realized by treating the crude reaction mixture with bases. Unfortunately, the trifluoroacetyl derivatives are unstable and their purification on silica gel

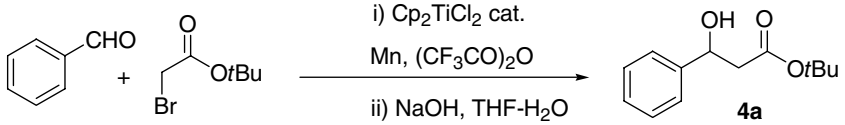


Scheme 1. Pinacol coupling of aromatic aldehydes promoted by low-valent titanium complexes.



Scheme 2. Titanium-catalyzed Reformatsky reaction in the presence of different titanium metal complexes and scavengers.

Table 1
Optimization of the Reformatsky reaction catalytic in titanium



Entry[a]	Solvent	Catalyst (mol%)	Yield[b] (%)
1	CH_3CN	10	60
2	THF	10	45
3	DMF	10	0
4[c]	CH_3CN	10	30
5	CH_3CN	5	22
6	CH_3CN	20	0
7	CH_3CN	30	0
8[d]	CH_3CN	10	10
9[e]	CH_3CN	10	0
10[f]	CH_3CN	10	30
11[g]	CH_3CN	10	0

[a] All the reactions were conduced at room temperature for 24 h using 1 equiv. of benzaldehyde, 1.5 equiv. of ester, 3 equiv. of Mn and 1.5 equiv. of $(CF_3CO)_2O$. The Cp_2TiCl_2 was used in 10 mol% in a concentration of 0.2 M with respect the reaction solvent.
[b] Isolated yield of the hydrolyzed product after chromatographic purification.
[c] Ethyl bromoacetate was used as reaction partner.
[d] Concentration of the titanium catalyst was 0.1 M.
[e] Concentration of the titanium catalyst was 0.4 M.
[f] 1 equiv. of $(CF_3CO)_2O$ was used as scavenger.
[g] 3 equiv. of $(CF_3CO)_2O$ were used as scavengers.

caused extensive decomposition. On the other hand the deprotection is quite sensitive to hindrance of the ester, and in the case of *tert*butyl, higher isolated yields were always observed.

The reaction is quite sensitive to concentration and quantity of the catalyst (Table 1, entries 8–10). In fact, performing the model reaction in the presence of more than 20 mol% of the titanium catalyst, and maintaining unaltered the other variables, no product was isolated. This was determined by the fast pinacol coupling occurring under these conditions. The concentration of the reaction is, on this respect, important. High concentration furnished the desired product in very low yield, while in diluted conditions, no reaction occurred. In Table 1 the effect of varying the equivalent of $(CF_3CO)_2O$ is also reported. Optimal yields were obtained when 1.5 equiv. of the reagent were employed. Lower quantities decreased the yield while an excess of anhydride promoted the pinacol coupling. The effect of the temperature of the reaction was also evaluated. Performing the reaction of benzaldehyde with different esters at 0 °C considerably reduced the isolated yield, sign of incomplete reaction. The general scope of the method was evaluated with a variety of aliphatic and aromatic aldehydes, and in Table 2 a collection of results is reported.

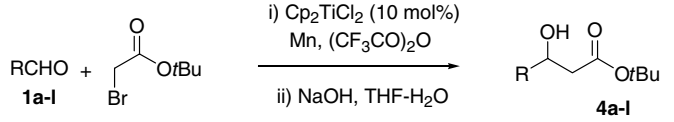
The aldehydes were completely consumed during the reactions, however, the isolated yields are showing that the concomitant pinacol coupling was reduced but not completely eliminated under the optimal reaction conditions. Moreover, a certain amount of aldehyde was present after deprotection, showing a probable retroaldol mechanism that was reducing the yield. Unfortunately all the attempts to use different deprotection schemes (i.e. LiOH, LiOOH) in order to improve yield failed.

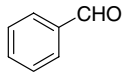
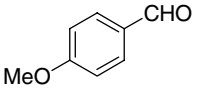
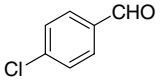
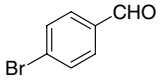
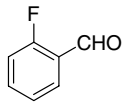
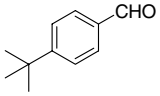
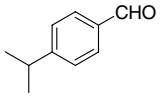
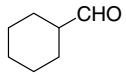
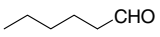
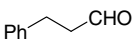
Tentatively, we propose for this Reformatsky reaction the catalytic cycle depicted in Fig. 1.

We believe that manganese enolates are not involved in our reaction. In fact, Rieke showed that activated Mn(0), prepared through the reduction of anhydrous Mn salts with lithium and naphthalene [26], was giving good yield in the corresponding Mn-mediated Reformatsky reaction. However, non activated Mn is reacting sluggishly with bromohalides.

Moreover, to exclude the intermediacy of Mn enolates in our process we have studied the model reaction in absence of titanium, using Me_3SiCl or $(CF_3CO)_2O$ as scavengers. Only in the presence of additive such as NaI and using Me_3SiCl, the desired product was isolated in 41% yield. In addition, Durandetti has reported that activated Mn can form enolate with bromoesters only with long reaction time (3–4 days), carrying out the reaction at 50 °C [27]. We can reasonably conclude that our process is controlled by titanium and the formation of titanium enolates is involved. In an attempt to develop stereocontrolled titanium catalyzed Reformatsky reaction, we have tested different chiral titanium complexes **5**–**7** (Scheme 3). The Duthaler–Hafner [28] titanium complex **5** is commercially available, the titanium catalyst **6** was prepared by the reaction conditions described by Joshi [29]. Finally, the titanium catalyst **7** was obtained *in situ* by addition of

Table 2
The titanium-catalyzed Reformatsky reaction with aromatic and aliphatic aldehydes



Aldehyde[a]	Product	Yield[b] (%)
	**4a**	60
	**4b**	32
	**4c**	50
	**4d**	40
	**4e**	30
	**4f**	40
	**4g**	50
	**4h**	40
	**4i**	48
	**4j**	32

[a] All the reactions were conduced at room temperature for 24–48 h using 1 equiv. of aldehyde, 1.5 equiv. of ester, 3 equiv. of Mn and 1.5 equiv. of $(CF_3CO)_2O$. The Cp_2TiCl_2 was used in 10 mol% in a concentration of 0.2 M to respect the reaction solvent.

[b] Isolated yield of the hydrolyzed product after chromatographic purification.

$Ti(OiPr)_4$ to the free ligand [30]. The systems **5**–**7** were chosen on the basis of the following considerations. The three titanium complexes are quite different in terms of coordination properties. The titanium enolates prepared by transmetallation from the Duthaler–Hafner reagent afford good facial selectivity with aldehydes in diethyl ether as the reaction solvent [31]. Quite interestingly, the stereoselection was independent by the reaction temperature in the limit of the isobutyraldehyde investigated. The Joshi's catalyst **6** is stable in the presence of Mn and scavengers, and it is able to give good stereoselection in the pinacol coupling, while the system **7** is stable in the presence of metal alcohoxydes.

The three chiral titanium catalysts promoted the titanium Reformatsky reaction with benzaldehyde, affording the desired product **4a** in 45%, 42% and 70% yield, respectively. Unfortunately, no enantiomeric excess was detected [32]. Titanium enolates formed in the reaction conditions can react through open transition state, in which a metal complex, acting as a Lewis acid, is activating the aldehyde, or they react through cyclic transition state, in which the

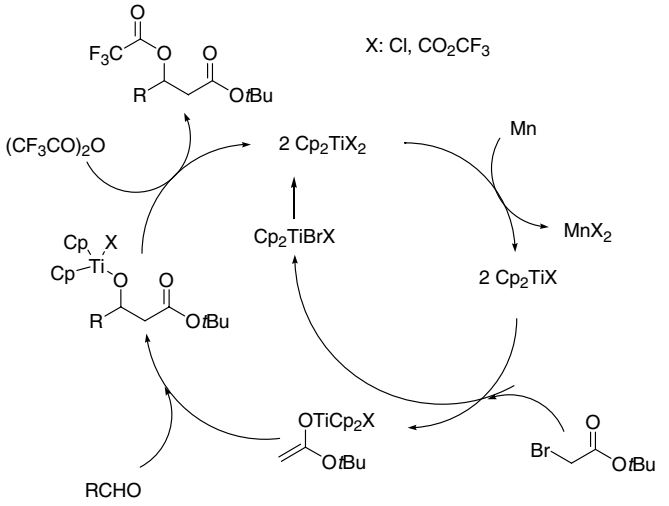
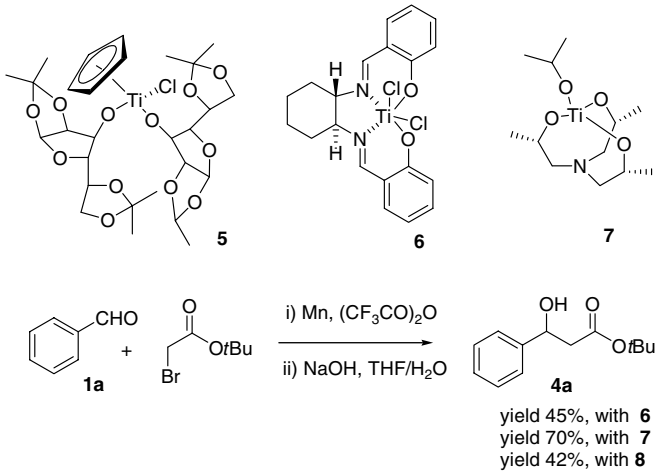


Fig. 1. Proposed catalytic cycle for the titanium-mediated Reformatsky reaction.



Scheme 3. Reformatsky reaction promoted by chiral titanium catalysts.

aldehyde and titanium enolate are coordinated by the same titanium atom. In addition, when cyclic transition states are possible, boat and chair transition state could be energetically available. Our Reformatsky reaction is probably occurring through the formation of a titanium enolate at room temperature. The presence of additive and Lewis acid salts, formed during the reaction course, open the access to many concomitant transition states making the Reformatsky reaction unselective. A more effective catalyst design in order to control the process with chiral titanium complex will be the object of further investigations.

3. Conclusion

In summary, we have described a truly catalytic titanium mediated Reformatsky reaction promoted by catalytic amount of Cp_2TiCl_2 or other titanium complexes. The combined use of stoichiometric amount of Mn as reductant, and of $(CF_3CO)_2O$ as a scavenger allowed moderate yields of the corresponding Reformatsky adducts to be obtained with aliphatic and aromatic aldehydes. First attempts to promote a catalytic enantioselective Reformatsky reaction with chiral titanium complexes were unsuccessful, but we are confident that the conditions described in this paper can guide we or other groups to reach this goal in a near future.

4. Experimental

4.1. General details

^{1}H NMR spectra were recorded on Varian 200 MHz or Varian 300 MHz spectrometers. chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ 7.27 ppm). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = dublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian 50 MHz and Varian 75 MHz spectrometers with complete proton decoupling. Mass spectra were performed at an ionizing voltage of 70 eV. Chromatographic purification was made with 240–400 mesh silica gel. Analytical gas chromatography (GC) was performed on a Hewlett-Packard HP 6890 gas chromatograph, with a flame ionization detector and split-mode capillary injection system, using a Crosslinked 5% PH ME Siloxane (30 m) column or a Megadex5 chiral (25 m) column. IR analysis were performed with an FT-IR spectrophotometer. IR spectra are expressed by wavenumbers (cm^{-1}). Analytical high performance liquid chromatography was performed on a liquid chromatograph equipped with a variable wave-length UV detector (deuterium lamp 100–600 nm), using a Daicel OD (0.46 cm ID × 25 cm) (Daicel Inc.). Anhydrous CH_3CN was purchased by Fluka. Mn, $(CF_3CO)_2O$ were used as received (Fluka, Aldrich). All aldehydes were freshly distilled by Kulgerorh apparatus before their use.

4.2. General procedure for the titanium-mediated Reformatsky reaction

In a two necked flask Cp_2TiCl_2 (0.05 mmol) was dissolved in CH_3CN (1.8 mL) then Mn (1.5 mmol) was added. The mixture was stirred 5–15 min. until the titanium complex was reduced (color turned into green). To the reaction mixture *tert*butyl bromoacetate (0.75 mmol) was added and the mixture was stirred for 1 h at room temperature, then the aldehyde (0.5 mmol) and trifluoroacetic anhydride (1.5 mmol) were added. The reaction mixture was stirred 24–36 h, then the mixture was quenched by water. The reaction mixture was filtered over celite© and extracted three times with Et_2O. The collect organic phases were evaporated under reduced pressure to give a dark yellow oil containing the crude trifluoroacetate esters. The oil was dissolved in THF (2 mL) and NaOH 1 M (1 mL) was added. The reaction mixture was stirred few minutes then diluted with H_2O. The aqueous mixture was extracted with Et_2O (3 × 4 mL) then the organic phases were reunited, dried over Na_2SO_4 and then evaporated under reduced pressure to give an oil purified by flash chromatography (eluant: *c*-Hex:Et_2O 9:1–8:2).

4.2.1. tertButyl-3-hydroxy-3-phenyl-propionate (**4a**)

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.13 (s, 9H); 2.64–2.68 (m, 2H); 3.47 (d, 1H, $J = 3.4$ Hz); 5.09 (m, 1H); 7.38–7.35 (m, 5H).

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 171.6; 142.6; 128.3 (×2); 127.5; 125.6 (×2); 81.3; 70.3; 44.3; 28.0.

IR (neat): 3447, 2979, 2931, 1727, 1150 (cm^{-1}).

GC–MS: 165 (22); 147 (8); 230 (6); 79 (54); 57 (88); 167 (7); 51 (22) (*m*/*z*).

(*R*)-*tert*Butyl-3-hydroxy-3-phenyl-propionate, $[\alpha]_D = +39.0°$ (*c* 1.24, $CHCl_3$) [32,33].

4.2.2. tertButyl-3-hydroxy-3-(4-methoxyphenyl)-propionate (**4b**)

^{1}H NMR ($CDCl_3$, 200 MHz): δ: 1.46 (s, 9H); 2.60–2.73 (m, 2H); 3.31–3.40 (br, 1H); 3.81 (s, 3H); 5.01–5.10 (m, 1H); 6.87–6.92 (m, 2H); 7.29–7.34 (m, 2H).

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 171.7; 158.9; 134.7; 126.9; 113.71; 81.4; 70.0; 52.2; 44.3; 28.1.

IR (neat) 3196, 2976, 2873, 1727, 1150 (cm^{-1}).

GC–MS: 234 (11); 178 (100); 161 (44); 133 (15); 77 (15); 57 (20) (*m*/*z*).

4.2.3. tertButyl-3-hydroxy-3-(4-fluorophenyl)-propionate (**4c**)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.45 (s, 9H); 2.61–2.65 (d, 2H, $J = 6.3$ Hz); 3.55–3.53(d, 1H, $J = 3.2$ Hz); 5.51–5.01 (m, 1H); 7.04 (t, 2H, $J = 8.6$ Hz); 7.34 (dd, 2H, $J = 8.2$, 8.1 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 171.6; 164.5; 159.6; 138.3 (d, $J = 12$ Hz); 127.4 (d, $J = 31$ Hz); 115.0 (d, $J = 85$ Hz): 81.5; 69.7; 44.3; 28.0.

IR (neat): 3439, 2980, 1725, 1153 (cm^{-1}).

GC–MS: 183 (27); 165 (9); 125 (100); 97 (30); 77 (13); 57 (95) (*m*/*z*).

4.2.4. tertButyl-3-hydroxy-3-(4-chlorophenyl)-propionate (**4d**)

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.45 (s, 9H); 2.64–2.68 (m, 2H); 3.47 (d, 1H, $J = 3.4$ Hz); 5.09 (m, 1H); 7.320–7.348 (m, 4H).

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 171.4; 141.1; 133.1; 128.4; 126.9; 81.6; 69.6; 44.1; 28.0.

IR (neat): 3447, 2979, 2931, 1727, 1150 (cm^{-1}).

GC–MS: 165 (22); 147 (8); 230 (6); 79 (54); 57 (88); 167 (7); 51 (22) (*m*/*z*).

4.2.5. tertButyl-3-hydroxy-3-(4-bromophenyl)-propionate (**4e**)

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.45 (s, 9H); 2.63–2.58 (m, 2H); 3.47 (d, 1H, $J = 3.2$ Hz); 5.09 (m, 1H); 7.27–7.23 (m, 2H); 7.49–7.45 (m, 2H).

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 171.6; 141.5; 131.3; 127.3; 121.2; 81.6; 69.6; 44.1; 28.0.

IR (neat): 3447, 2979, 2931, 1727, 1150 (cm^{-1}).

GC–MS: 165 (22); 147 (8); 230 (6); 79 (54); 57 (88); 167 (7); 51 (22) (*m*/*z*).

4.2.6. tertButyl-3-hydroxy-3-(2-fluorophenyl)-propionate (**4f**)

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.46 (s, 9H); 2.71–2.65 (m, 2H); 3.70 (d, 1H, $J = 3.6$ Hz); 5.40 (dd, 1H, $J = 3.6$, 8.4 Hz); 7.03 (t, 1H, $J = 8.7$ Hz); 7.16 (t, 1H, $J = 7.2$ Hz); 7.27–7.26 (m, 1H); 7.54 (t, 1H, $J = 7.5$ Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 171.6; 160.9; 158.1; 129.2 (d, $J = 45$ Hz); 128.8 (d, $J = 33$ Hz); 127.1 (d, $J = 17$ Hz); 124.1 (d, $J = 13$ Hz); 115.1 (d, $J = 85$ Hz); 81.5; 64.5; 42.8; 28.0.

IR (neat): 3469, 2979, 2932, 1717, 1152 (cm^{-1}).

GC–MS: 184 (11); 125 (72); 97 (22); 77 (17); 57 (100); 51 (22) (*m*/*z*).

4.2.7. tertButyl-3-hydroxy-3-(4-tertbutylphenyl)-propionate (**4g**)

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.30 (s, 9H); 1.44 (s, 9H); 2.63–2.65 (m, 2H); 3.27 (d, 1H, $J = 3.0$ Hz); 5.09 (m, 1H); 7.35–7.26 (m, 4H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 171.6; 150.4; 139.6; 125.4; 125.2; 81.3; 70.2; 44.3; 34.5; 31.3; 28.1.

IR (neat) 2972, 2924,1707, 1050 (cm^{-1}).

GC–MS: 221 (16); 161 (100); 147 (21); 119 (10); 105 (20); 91 (27); 77 (10); 57 (81) (*m*/*z*).

4.2.8. tertButyl-3-hydroxy-3-(4-isopropylphenyl)-propionate (**4h**)

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.28 (d, 6H, $J = 6.8$ Hz); 1.49 (s, 9H); 2.72–2.68 (m, 2H); 2.98 (sept, 1H, $J = 6.8$ Hz); 3.40 (br s, 1H); 5.12 (m, 1H); 7.36–7.23 (m, 4H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 171.8; 148.2; 139.9; 126.4; 125.6; 81.3; 70.3; 44.2; 33.1; 30.9; 28.1; 23.9.

IR (neat): 3447, 2979, 2931, 1727, 1150 (cm^{-1}).

GC–MS: 165 (22); 147 (8); 230 (6); 79 (54); 57 (88); 167 (7); 51 (22) (*m*/*z*).

4.2.9. tertButyl-3-hydroxy-3-cyclohexyl-propionate (**4i**)

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.50–1.00 (m, 7H); 1.48 (s, 9H); 2.55–2.20 (m, 2H); 3.10 (d, 1H, $J = 3.2$ Hz); 3.82 (m, 1H).

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.9; 81.1; 72.18; 43.0; 36.5; 28.7; 28.3; 28.1; 28.5; 27.0; 26.2.

IR (neat) 3447, 2979, 2931, 1727, 1150 (cm^{-1}).

GC–MS: 165 (22); 147 (8); 230 (6); 79 (54); 57 (88); 167 (7); 51 (22) (*m*/*z*).

4.2.10. tertButyl-3-hydroxy-3-nhexyl-propionate (**4j**)

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 0.92 (t, 3H, $J = 7.2$ Hz); 1.80–1.10 (m, 10H); 1.42 (s, 9H); 2.35 (dd, 1H, $J = 6.0$, 11.0 Hz); 2.42 (dd, 1H, $J = 2.2$, 11.0 Hz); 3.1 (br s, 1H); 4.09–3.94 (m, 1H).

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.3; 81.0; 68.0; 42.3; 36.4; 31.7; 28.1; 25.1; 22.6; 14.0.

IR (neat): 3447, 2979, 2931, 1727, 1150 (cm^{-1}).

GC–MS: 165 (22); 147 (8); 230 (6); 79 (54); 57 (88); 167 (7); 51 (22) (*m*/*z*).

4.2.11. tertButyl-3-hydroxy-3-(3-phenylpropyl) propionate (**4k**)

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.46 (s, 9H); 1.90–1.60 (m, 2H); 2.45–2.30 (m, 3H); 2.90–2.60 (m, 2H); 4.20–3.90 (m, 1H); 7.36–7.14 (m, 5H).

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 171.6; 142.6; 128.3; 127.5; 125.6; 81.3; 70.3; 44.3; 30.9; 28.0.

IR (neat): 3447, 2979, 2931, 1727, 1150 (cm^{-1}).

GC–MS: 165 (22); 147 (8); 230 (6); 79 (54); 57 (88); 167 (7); 51 (22) (*m*/*z*).

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