Green Chemistry

PAPER

An eco-sustainable erbium(III)-catalyzed method for formation/cleavage of *O-tert*-butoxy carbonates†

Antonio Procopio,*[a] Giancarlo Cravotto,[b] Manuela Oliverio,[a] Paola Costanzo,[a] Monica Nardi[c] and Rosina Paonessa[a]

A new simple and effective method for the formation/cleavage of *O-tert*-butoxy carbonates of alcohols and phenols is proposed. Mesoporous silica-supported Er(III) (Er^{III}-MCM-41) was used as an efficient and reusable solid catalyst in the solvent-free ultrasound-assisted synthesis of Boc-carbonate derivatives of a wide range of alcohols and phenols. The fast, selective deprotection of Boc-derivatives is achieved with a very low amount of Er(OTf)$_3$ in ethanol under microwave irradiation. Therefore, the entire protection/de-protection process is very attractive, from the point of view of sustainability.

Introduction

In the last decade, the investigation and application of Green Chemistry principles has led to the development of many new technologies devoted to cleaner and more benign chemical processes.[1,2] Basically, Green Chemistry utilizes a set of principles which aim to downsize the energy consumption and reduce or eliminate the use or generation of hazardous substances in the design, manufacture and application of chemical products (non-classical forms of energy including radiofrequency or microwave (MW) irradiation and sonochemistry, solvent-free reaction, recyclable solid catalysts, environmental benign solvents, *etc.*).[3–6] From this point of view, the chemoselective transformation of multifunctional organic compounds still presents a severe challenge for the organic chemists and the success of a multi-step synthesis depends, very often, on efficient manipulation of the functional groups involved. Organic carbonates are an important class of compounds of pharmacological and chemical importance,[7] additionally, *tert*-butoxy carbonates (Boc) are also extensively used as protecting groups in the chemical synthesis of complex molecules.[8] In this context, the commercially available di-*tert*-butyl dicarbonate (Boc$_2$O) is a better choice for preparing organic carbonates

by direct coupling with hydroxy compounds in the presence of a catalyst. However, most of the methods reported above employ homogeneous catalysts, which are not easily reusable and, in any case, cannot be considered fully acceptable from the point of view of sustainability.[8-10] Moreover, of the many efforts recently devoted to developing more environmentally friendly procedures for their synthesis,[10] only very few use a heterogeneous catalyst.[9k,l] Thus, there is still a need to develop an efficient catalytic protocol that could overcome the above disadvantages and facilitate the *O-tert*-butoxycarbonylation of various hydroxy compounds under milder reaction conditions. As a continuation of our previous work aimed at developing new catalytic methods for valuable protection/deprotection steps of functional groups,[11] we herein report a simple and eco-friendly method for the formation/cleavage of *O*-Boc-derivatives of hydroxyl compounds.

Results and discussion

We have recently reported a MW assisted protocol for the rapid and efficient, solvent-free functionalisation of mesoporous silica MCM-41. The methodology described can be applied to several different functional groups, and can be potentially employed for different applications since the loading can be tuned by simply choosing the appropriate MW-dielectric heating time. Thus, developing this methodology, we have designed a fast, cheap MW-assisted method to synthesize a new environmentally friendly mesoporous silica-supported Er(III) catalyst (Er^{III}-MCM-41) while also demonstrating that this is a very efficient reusable solid catalyst in the cyanosilylation of carbonyl compounds.[12] We have now decided to test the potential use of this heterogeneous catalyst in the reaction between hydroxyl compounds and di-*tert*-butyl-dicarbonate (Boc anhydride). As

[a]*Dipartimento Farmaco-Biologico, Università degli Studi della Magna Græcia Complesso Ninì Barbieri, 88021, Roccelletta di Borgia, (CZ), Italy. E-mail: procopio@unicz.it; Fax: +39 0961 369 5713; Tel: +39 0961 369 4120*
[b]*Dipartimento di Scienza e Tecnologia del Farmaco Università di Torino Via Giuria 9, 10125, Torino, (Italy)*
[c]*Dipartimento di Chimica, Università della Calabria, Ponte Bucci, 87030, Arcavacata di Rende, (CS), Italy*
† Electronic supplementary information (ESI) available: See DOI: 10.1039/c0gc00728e

reported by Bartoli et al.,[13] the reaction between alcohols and Boc$_2$O leads to the formation of *tert*-butyl ethers and/or Boc-derivatives, depending of the nature of the Lewis acid catalyst. Thus, in order to investigate product distribution, preliminary experiments were carried out on the model reaction between 4-methoxyphenol (**1**) and Boc$_2$O in solvent free conditions at room temperature (Scheme 1).

Scheme 1
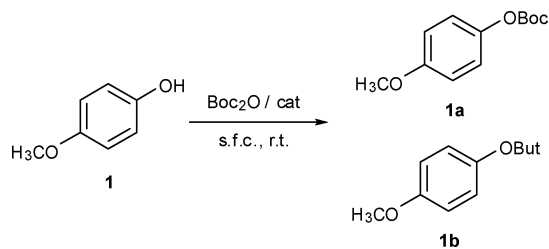
Initially, the reaction was performed under catalyst-free conditions and no product formation was observed (entry 1 in Table 1). The same reaction performed adding Er(OTf)$_3$ as homogeneous catalyst gave the corresponding *tert*-butyl ether **1b** and an inextricable mixture of *tert*-butyl carbonate **1a** and electrophilic aromatic substitution by-products, as shown by the GC-MS spectra examination (entry 2 in Table 1). Surprisingly, the reaction of 4-methoxyphenol (**1**) with Boc anhydride catalyzed by the heterogeneous catalyst Er^{III}-MCM-41 (10 mol%) in solvent free conditions gave the corresponding *tert*-butyl carbonate **1a** as the major product with only 2% of *tert*-butyl ether **1b** (entry 3 in Table 1). Bartoli et al. [13] clearly observed the influence of the anion in product distribution concluding that dissociated salts gave *tert*-butyl ethers, whereas intimate ion pairs led to Boc-alcohols. They explained this trend in term of the HSAB theory. Therefore, the "soft" triflate does not match with the trivalent metal cations generally considered to be "hard" and, as a consequence, triflates mostly give *tert*-butyl ethers. Conversely, in the case of the Er^{III}-MCM-41 solid

catalyst (Scheme 1), which still contains the triflate counterion, the Boc-derivative was exclusively obtained (entry 4 in Table 1). Taking into account the observations reported by Bartoli et al. and our experimental results, we hypothesized that the freer the Lewis acid centre is, the more it can coordinate the initially produced Boc-carbonate inducing a decarboxylation process which furnishes the *tert*-butyl ether. In the case of the Er^{III}-MCM-41 catalyst, the limited degrees of freedom stop the erbium(III) cation carrying out the described process, leaving the Boc-carbonate **1a** as the only product of the reaction pictured in Scheme 1. Thus, examining the data reported in Table 1, it emerges that the best experimental conditions to perform the reaction, as described in Scheme 1, include the use of 20 mol% of Er^{III}-MCM-41 catalyst at room temperature for 24 h to obtain the quantitative conversion of substrate **1** and the formation of *tert*-butyl carbonate **1a** as the only product (entry 4, Table 1). The well known instability of Boc$_2$O in the prolonged experimental conditions made a 2.3 molar excess of this reagent necessary.[14] In fact, a lower amount of Boc$_2$O only gave modest product percentages **1a** (entries 5–6 in Table 1). Analogously, the attempt to perform the reaction in a shorter time failed and only furnished an average product yield (entry 7, Table 1). Interestingly, it has been reported that in many heterogeneous reactions the application of ultrasound (US) has the same effect as a high-speed stirrer or a homogenizer and that enhanced yields and rates can be observed because of the mechanical effects of shock waves.[15] Astonishingly, when the reaction reported in Scheme 1 was performed under US assistance, we obtained complete substrate conversion (**1**) after only 1 h with the exclusive quantitative formation of the *tert*-butyl carbonate **1a** (entry 8, Table 1). We further investigated the reusability of the catalyst which was filtered from the reaction mass, washed and dried under vacuum.

Then, we verified that ultrasound exposure did not cause loss of Er(III) or significant structural modification of the recovered Er^{III}-MCM-41 solid catalyst (Table 2, see also ESI†) before we reused it for another four consecutive cycles with no significant loss of activity (entry 9 in Table 1). As a matter of fact, the ICP-MS analysis performed on the filtered solution after one US-assisted reaction cycle showed a Er(III) leaching of only 0.0139%. Lastly, good conversion of substrate **1** was registered performing the reaction reported in Scheme 1 at 40 °C without the ultrasound assistance, but only after a prolonged reaction time (entry 10 in Table 1).

To fully exploit the general utility of the present method, we applied the optimized reaction conditions described in entry 8 Table 1 to a wide variety of alcohols and phenols (Scheme 2 and Table 3). Notably, a small amount of Boc-derivatives were obtained when the reaction was carried out at room temperature on aliphatic substrates (entries 1–4, Table 3) even after prolonged reaction times, whereas high yields of

Table 1 Screening of the experimental conditions for reactions of Scheme 1 catalyzed by Er^{III}-MCM-41

Entry	Boc$_2$O (eq.)	Catalyst (mol%)^c	Time (h)	Conv. (%)	1a : 1b^a (% yield)
1	2.3	0	24	—	—
2	2.3	0.5^b	24	82	0 : 76
3	2.3	0.5	24	60	58 : 2
4	2.3	1.0	24	100	99 : 0
5	1.0	1.0	24	66	52 : 2
6	1.5	1.0	24	78	47 : 15
7	2.3	1.0	12	54	48 : 0
8	2.3^d	1.0	1	100	100 : 0
9	2.3^d	1.0	1	98	100 : 0
	2.3^d	1.0	1	98	100 : 0
	2.3^d	1.0	1	96	100 : 0
	2.3^d	1.0	1	95	100 : 0
10	2.3^e	1.0	2	99	96

^{a} Conversion and yield were determined by GC-MS using **1a** and **1b** in the standard addition method. ^{b} Er(OTf)$_3$ was used as catalyst in 10 mol%. ^{c} Er^{III}-MCM-41 was used as catalyst and the mol% was calculated on the basis of the analytical data reported in the reference 12a. ^{d} Reaction performed under ultrasound irradiation T max 40 °C. ^{e} Reaction performed without ultrasound irradiation at 40 °C.

Table 2 Structural examination of Er^{III}-MCM-41 solid catalyst before and after ultrasound exposure

| Er^{III}-MCM-41	SBET (m²/gr)	Pore volume (P/P$_0$ = 0.9) (cm³/gr)	ICP-MS (mmol Er(III)/gr)
Before-US	575	0.41	0.8
After-US	416	0.283	0.7999
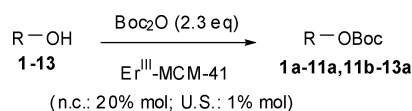
Scheme 2

tert-butoxy carbonates were obtained with short reaction times in the case of phenols (entries 5–10 in Table 3). In those circumstances, no substantial differences in reactivity were noted for electron-rich and electron-poor aromatic substrates.

The extraordinarily positive influence of US irradiation was confirmed for all the reported examples and, as a matter of fact, almost quantitative yields were observed when the reaction of *tert*-butoxy carbonate formation was performed under the action of US for most of the reported examples in Table 3. Remarkably, the application of US irradiation was decisive for aliphatic alcohols, giving very high Boc-derivative yields even in the case of substrates which showed no- or low-reactivity in ordinary conditions (entries 1–4 in Table 3), or in complex substrates such as the lateral chain of Boc-tyrosine methyl ester **10** (entry 10 in Table 3).

At the end of the reaction, the excess of Boc anhydride, which is very difficult to separate from the products, must be reduced to an unreactive species and eliminated from the reaction mixture before the chromatographic purification of the product. The application of US irradiation showed its enormous utility in that case too, permitting the complete degradation of the Boc anhydride by reaction with 2,2,2-trifluoroethanol in only 20 min at room temperature without the concomitant deprotection of the Boc-carbonate produced.

An intriguing example was found among the substrates reported in Table 3. Homovanillic alcohol **11** is so insoluble at room temperature that it was completely unreactive in the conventional reaction conditions. Nevertheless, when the reaction between **11** and Boc anhydride was carried out following the US-assisted protocol, a high percentage of conversion of the substrate was registered after only 1 h furnishing the mono-Boc-derivative **11a** (Scheme 3) as the unique product of the reaction. No other changes in the profile of the reaction were observed even after a prolonged reaction time. Taking into account that two reactive hydroxyl groups are present on the substrate, we planned to perform the reaction using a higher amount of Boc$_2$O. In that case, we again observed the complete conversion of the substrate **11** in only 1 h, but the initially formed product **11a** was slowly converted to the di-Boc-carbonate derivative **11b** (entry 11 in Table 3) that was the only remaining product of the reaction after 9 h. This last result clearly disagrees with the data reported in Table 3, where the phenolic functionalities are
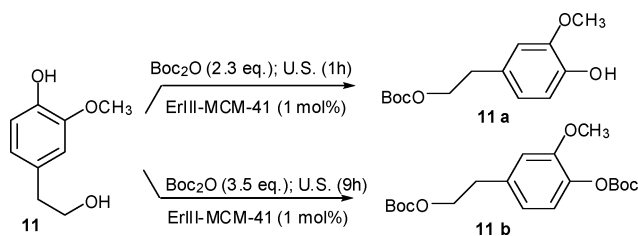
always more reactive than the alcoholic hydroxyl groups in the reaction reported in Scheme 2.

The divergent behavior could be reasonably explained by the steric hindrance of the phenolic group on the homovanillic alcohol. This is confirmed by the trend seen comparing the results of the reaction performed on substrate **1** and its positional isomer 2-methoxyphenol **12** and on the positional isomers of cresol (entries 7, 12–14 in Table 3) where the guaicol **12** and *o*-cresol **13** resulted significantly less reactive than *p*-isomers **1** and **14** especially when the reaction was carried on without US. The US-assisted Boc-protection of alcohols and phenols using a reusable heterogeneous solid catalyst in solventless conditions can be seen as a significant step forward in green chemistry. However, it can only be considered truly valuable if an equally effective deprotection method is available. Therefore, considering the reported performance of erbium(III) as the Lewis acid catalyst in several protection/deprotection protocols,[11] we screened the best experimental conditions in which to perform the deprotection of the *tert*-butyl carbonates reported in Table 3 using the model substrate **1a** (Table 4 and Scheme 4).
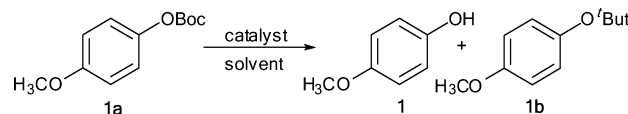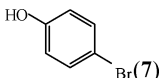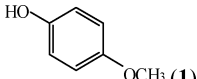

Scheme 4
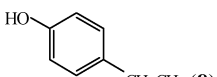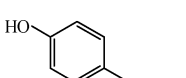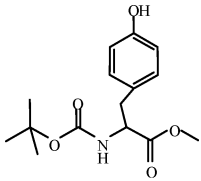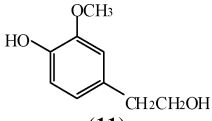
Initially, we tested the solid catalyst Er^{III}-MCM-41, but it was not able to perform the cleavage of the *tert*-butoxy protecting group from the derivative **1a** in refluxing acetonitrile even with a prolonged reaction time (entry 1, Table 4). Furthermore, an average yield was observed when a double quantity of solid catalyst was employed. This procedure furnished a mixture of the phenol **1** and its *tert*-butyl ether **1b** as by-products (entry 2, Table 4).
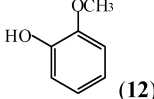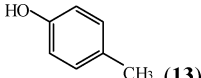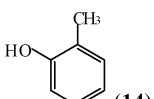
Conversely, the deprotection reaction carried out in the same experimental conditions using 10 mol% of Er(OTf)$_3$ as a catalyst gave a quantitative conversion of the substrate **1a** into the deprotected phenol **1** in only 1 h and with only 18% of by-product **1b**. Nearly the same result was observed when the amount of catalyst was reduced to only 5 mol%, whereas lower percentages or no conversion was observed when the reaction temperature was lowered (entries 4–6 in Table 4).

A quantitative transformation of the substrate was also registered in several others refluxing solvents (entries 7–10, 13 in Table 4) but, it is worth noting that the amount of by-product **1b** was negligible only in polar solvents (entries 8, 10 and 13 in Table 4). Good results were still obtained in refluxing nitromethane and ethanol lowering the mol% of Er(OTf)$_3$ (entries 11, 12 and 14, 15 in Table 4). More specifically, in nitromethane 1 mol% of catalyst was sufficient to provide a quantitative conversion of the *tert*-butyl carbonate **1a**.

Unfortunately, the attempt to reproduce similar results in the much greener ethanol failed (entry 15 in Table 4) and, comparable results in this solvent were registered only using 5 mol% catalyst for a prolonged reaction time (entry 14 in Table 4). As previously reported,[12] the use of MW heating again allowed us to develop a greener reaction protocol.

Scheme 3

Table 3 Synthesis of Boc alcohols catalyzed by 20 mg of Er^{III}-MCM-41 (1 mol%) using 2.3 eq. of Boc anhydride under solvent-free conditions

Entry	Substrate	T (°C)	Time (h)	Conv. (%)	Yield (%)^a
1	$CH_3(CH_2)_7OH$ (**2**)	rt	24	27	—
		US^b	2.5	quant	81
2	$CH_3CH(OH)CH_2CH_3$ (**3**)^c	rt	24	—	—
		US^b	2.5	quant	75
3	$CH_2{=}CH(CH_2)_3OH$ (**4**)	rt	24	10	10
		US^b	3	quant	quant
4	cyclohexanol (**5**)	rt	24	15	—
		US^b	5	92	97
5	phenol (**6**)	rt	5	98	73 (88)^d
		US^b	1	quant	quant
6	4-bromophenol (**7**)	rt	5	98	97
		US^b	1	quant	quant
7	4-methoxyphenol (**1**)	rt	24	quant	99
		US^b	1	quant	quant
8	4-ethylphenol (**8**)	rt	24	97	89
		US^b	1	quant	quant
9	4-nitrophenol (**9**)	rt	24	90	85
		US^b	1	quant	quant
10	Boc-Tyr-OMe (**10**)	rt^e	24	20	—
		US^{b,g}	1	quant	quant
11	(**11**)	rt^e	24	—	—
		US^b	1	90	85^f
		US^{b,h,i}	9	quant	92^g
12	2-methoxyphenol (**12**)	rt	24	60	60
		US^b	2	98	98
13	4-methylphenol (**13**)	rt	24	78	77
		US^b	1.5	quant	99
14	2-methylphenol (**14**)	rt	24	56	53
		US^b	1.5	quant	97

^{a} Isolated yields; all the compounds, when necessary, were purified by flash chromatography, and characterized by ^{1}H NMR and EI-MS. ^{b} Reaction performed under ultrasound irradiation T max 40 °C. ^{c} Volatile compound, identification by GC-MS. ^{d} Yield determined by GC-MS analysis. ^{e} US-assisted solubilization of partially miscible reagents at r.t. ^{f} Referred to the mono Boc-alcholic derivative, no changes in the reaction profile were observed after 24 h. ^{g} Referred to di-Boc derivative. ^{h} A double amount of Boc anhydride was used. ^{i} 3.5 eq. of Boc anhydride were used.

Table 4 Screening of the experimental conditions for deprotection of *tert*-butyl carbonate **1a**

Entry	Solvent	Catalyst (mol%)	T (°C)	Time (min)	Conv. (%)	Yield (%) **1a** : **1b**
1	CH₃CN	Er[III]-MCM-41 (1)	80	300	0	0
2	CH₃CN	Er[III]-MCM-41 (2)	80	120	48	18 : 26
3	CH₃CN	Er(OTf)₃ (10)	80	60	quant	81 : 18
4	CH₃CN	Er(OTf)₃ (5)	80	60	quant	78 : 20
5	CH₃CN	Er(OTf)₃	40	300	60	24 : 26
6	CH₃CN	Er(OTf)₃	r.t.	180	0	0
7	Toluene	Er(OTf)₃ (10)	110	360	quant	79 : 20
8	Methanol	Er(OTf)₃	65	180	quant	95 : 4
9	CHCl₃	Er(OTf)₃	60	360	quant	50 : 50
10	CH₃NO₂	Er(OTf)₃	101	60	quant	94 : 1
11	CH₃NO₂	Er(OTf)₃ (5)	101	60	quant	96 : 2
12	CH₃NO₂	Er(OTf)₃ (1)	101	60	quant	96 : 2
13	Ethanol	Er(OTf)₃ (10)	78	60	quant	97 : 3
14	Ethanol	Er(OTf)₃ (5)	78	90	quant	94 : 3
15	Ethanol	Er(OTf)₃ (1)	78	180	30	22 : 0
16	CH₃NO₂[a]	Er(OTf)₃ (1)	80	15	quant	99 : 0
17	Ethanol[a]	Er(OTf)₃ (5)	80	15	quant	97 : 3
18	H₂O[a]	Er(OTf)₃ (10)	80	25	quant	99 : 0
19	Ethanol[a]	Er(OTf)₃ (1)	80	25	quant	98 : 1
		1° recycl.	80	25	quant	96 : 0
		2° recycl.	80	25	quant	95 : 0
		3° recycl.	80	25	quant	95 : 0
		4° recycl.	80	25	quant	93 : 1
20	Ethanol[a]	0	80	25	—	—

[a] Reaction performed under MW-assistance.

The MW-assisted reactions were performed in a Synthos 3000 instrument from Anton Paar using a temperature-controlled program.[16] Thus, the MW-assisted deprotection of *tert*-butyl carbonate **1a** gave a quantitative conversion of the substrate in all tested solvents (entries 16–19 in Table 4).

It is worth noting that the reaction also proceeded well in water, where the substrate **1a** was also insoluble under traditional reflux.

Most of all, under these conditions, only 1 mol% of catalyst was needed to obtain a nearly quantitative yield of deprotected phenol **1** after only 25 min (entry 19, Table 4). Moreover, after the completion of reaction, the ethanolic solution containing the catalyst was evaporated, fresh substrate was added and the process was repeated for four more cycles with consistent activity (entry 19, Table 4).

Finally, no reaction was observed when the reaction was carried out under the same experimental conditions but in absence of catalyst (entry 20, Table 4). Taking into account the yields, the reaction times and the toxicity of the solvents, the best compromise seemed to be performing the reaction in ethanol using 1 mol% of Er(OTf)₃ under MW-irradiation at 80 °C.

Excellent yields of deprotected hydroxyl substrates **1–14** were registered in very short reaction times applying the optimized experimental conditions above reported to *tert*-butyl carbonates **1a–14a** and **11b** (Table 5).

Conclusions

The proposed protocol enables the efficient *t*-Boc protection/deprotection of a wide range of alcohols and phenols in high yields and short reaction times. The convenient solvent-free sonochemical conditions and the reuse of the solid cat-
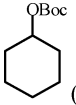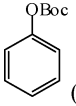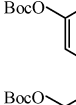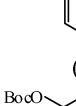
alyst (Er[III]-MCM-41) in the protection step, as well as the MW-assisted deprotection with very low amounts of reusable Er(OTf)₃ catalyst in ethanol, make the entire process in line with principles of green chemistry: This gives us a means of utilizing the Boc protection of the hydroxyl functionality in a truly environmentally sustainable way.
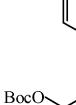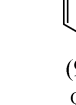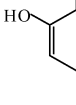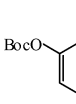
Experimental

General

[1]H spectra were recorded on a Bruker WM 300 instrument on samples dissolved in CDCl₃. Chemical shifts are given in parts per million (ppm) from tetramethylsilane as the internal standard (0.0 ppm). Coupling constants (J) are given in Hertz. Reactions were monitored by a GC-MS Agilent workstation, formed of a GC-6890N (30-m RESTEK-5SIL capillary column, working on splitless mode, 1 mL min⁻¹ He as carrier gas) and an 5973 N mass detector. The characterization of the porous structure was obtained by N₂ adsorption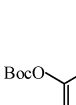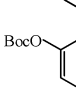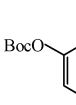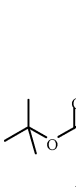/desorption isotherms, measured at 77 K on a Micromeritics ASAP 2010 volumetric adsorption analyser. Before measurements, samples were outgassed at 393 K for 6 h. These isotherms were used to evaluate BET specific surface area, pore volume and pore size distributions. The pore size distribution has been calculated using an algorithm based on the BJH theory. ICP-MS measures were performed in a quadrupole-based ICP-MS system XSERIES 2 ICP-MS, from Thermo Fisher Scientific, working in standard mode. Samples were introduced in a quartz concentric nebulizer by a peristaltic pump (selected speed of 30 rpm). The element concentration was determined against external calibration using a synthetic acid multielement calibration standard. MW-assisted reactions were performed

Table 5 MW assisted deprotection of of Boc derivatives **1a–13a**, **11b** catalyzed by Er(OTf)$_3$ (1 mol%) in ethanol

Entry	Substrate	Time (h)	Conv. (%)	Yield (%)[a]
1	CH$_3$(CH$_2$)$_7$OBoc (2a)	25[b]	quant	95
2	CH$_3$CH(OBoc)CH$_2$CH$_3$ (3a)	50	quant	98
3	CH$_2$=CH(CH$_2$)$_3$OBoc (4a)	24	quant	92
4	(5a)	50[b]	92	96
5	(6a)	25	95	93
6	(7a)	25	quant	quant
7	(1a)	25	quant	quant
8	(8a)	25	95	91
9	(9a)	25	quant	quant
10	(11a)	50[b]	90	94
11	(11b)	50[b]	quant	98
12	(12a)	25	quant	99
13	(13a)	25	95	94
14	(14a)	25	quant	97
15	(10a)	50	84	77[c]

[a] Isolated yields; all the compounds, when necessary, were purified by flash chromatography and the major product was fully characterized by the comparison of their spectral data with known compounds. [b] Reaction performed using 5 mol% of catalyst. [c] Referred to the Boc-tyrosine methyl ester **10**, with only 4% yield of completely deprotected NH$_2$-tyrosine methyl ester.

on a Synthos 3000 instrument from Anton Paar, equipped with a 64MG5 rotor and an IR probe as external control of the temperature. Using a temperature controlled program the instrument is able to tune the power magnetron in order to reach and to maintain the fixed temperature throughout the experiment. For each run 16 positions of the rotor were occupied by 0.3–3 ml glass vials sealed with a dedicated PEEK screw-cup together with a reliable PTFE seal. US reaction were performed in an ultrasound bath ULTRASONIC 06 from Falc (Power 40 W, frequency out 45/55 KHz). TLC were performed using silica plates 60-F264 on alumina, commercially available from Merk. Liquid Flash chromatography was performed on a Supelco VERSA FLASH HTFP station on silica cartridges commercially available from Supelco. All solvents were distilled before use by standard methods. All chemicals were used as commercially available.

Synthesis of *tert*-butyl carbonates

Room temperature synthesis of *tert*-butyl carbonates. In a general procedure 2.0 mmol of alcohol was dissolved in 2.3 eq of di-*tert*-butyl dicarbonate under soft heating (T < 40 °C). 20 mg of Er^{III}-MCM-41 (1% mol of Er(III)) was added to the mixture under N$_2$ atmosphere and the mixture was stirred at room temperature for 24 h. The reaction was monitored by TLC or GC-MS. On completion, the mixture was diluted with diethyl ether, the catalyst was filtered off and the solvent was evaporated under vacuum. Trifluoroethanol (3 ml) was added and the solution was sonicated in a US bath for 30 min to decompose the excess of di-*t*-butyl dicarbonate. The solvent was evaporated under vacuum and desired pure product was separated from the crude by flash chromatography. The catalyst was washed three times with ether, dried under vacuum and reused for the next run.

US-assisted synthesis of *tert*-butyl carbonates. In a general procedure 2.0 mmol of alcohol was dissolved in 2.3 eq of di-*t*-butyl dicarbonate under soft heating (T < 40 °C). Er^{III}-MCM-41 (20 mg, 1 mol% of Er(III)) was added to the mixture under N$_2$ atmosphere and sonicated in an US bath for 1 up to 5 h. The reaction was monitored by TLC or GC-MS. On completion, the mixture was diluted with diethylether, the catalyst was filtered off and the solvent was evaporated under vacuum. Trifluoroethanol (3 ml) was added and the solution sonicated in a US bath for 30 min to decompose the excess of di-*t*-butyl dicarbonate. The solvent was evaporated under vacuum and the desired pure product was separated from the crude by flash chromatography. The catalyst was washed three times with ether, dried under vacuum and reused for the next run.

***tert*-Butyl-4-methoxyphenyl carbonate (1).** Yield 99%; Rf (petroleum ether-diethylic ether 9 : 1) 0.50; δ (ppm)(300 MHz, CDCl$_3$): 1.55 (s, 9H, OtBut), 3.78 (s, 3H, OCH$_3$), 6.87 (ddd, 2H, H$_C$, H$_B$, J$_{orto}$ = 8 Hz, J$_{meta}$ = 1.99 Hz, J$_{para}$ = 1.80 Hz), 7.06 (ddd, 2H, H$_A$, H$_D$, J$_{orto}$ = 8.Hz, J$_{meta}$ = 1.99 Hz, J$_{para}$ = 1.80 Hz); m/z: 224 [M]$^+$, 209 [M–CH$_3$]$^+$, 124 [M–COOtBut+H]$^+$, 109 [M–CH$_3$–COOtBut+H]$^+$, 57 [tBut]$^+$.

***tert*-Butyl-octyl carbonate (2).** Yield 71%; Rf (petroleum ether-diethylic ether 97.5 : 2.5) 0.66; δ (ppm)(300 MHz, CDCl$_3$): 0.88 (t, 3H, CH$_3$, J$_{CH3CH2}$ = 6.5 Hz), 1.17–1.44 (m,8H,

2 × CH$_2$),1.48 (s, 9H, OtBut), 1.58 – 1.71 (m, 4H, 2 × CH$_2$), 4. 05(t, 2H, CH$_2$OBoc, J_{CH2CH2} = 6.86 Hz); m/z: 113 [M–CO$_2$–OtBut]$^+$, 112 [M–CO$_2$–HOtBut]$^+$, 57 [t-but]$^+$

sec-Butyl-*tert*-butyl carbonate (3). Yield 50%; volatile compound; m/z = 119 [M–isobutene]$^+$, 57 [t-but]$^+$.

tert-Butyl-pent-4-enyl carbonate (4). Yield 99%; Rf (petroleum ether-diethylic ether 8 : 2) 0.72; δ (ppm)(300 MHz, CDCl$_3$): 1.38 (s, 9H, -OtBut), 1.67–1.81 (m, 2H, H$_2$), 2.09–2.19 (m, 2H, H$_3$), 4.07 (t, 2H, H$_1$, J_{H1H2} = 6.83 Hz), 4.96–5.10 (m, 2H, H$_5$, H$_{5'}$); 5.73–5.88 (m, 1H, H$_4$) m/z = : 130 [M–tBut]$^+$, 69 [M–COOtBut]$^+$, 57 [tBut]$^+$.

tert-Butyl-cyclohexyl carbonate (5). Yield 92%; δ (ppm)(300 MHz, CDCl$_3$): 1.48 (s, 9H, OtBut), 1.22–1.62 (m, 6H, 2 × H$_3$, 2 × H$_4$, 2 × H$_5$), 1.74–1.78 (m, 2H, H$_2$, H$_{2'}$), 1.93–1.96 (m, 2H, H$_6$, H$_{6'}$), 4.48–4.57 (m, 1H, H$_1$); m/z: 145 [M-isobutene]$^+$, 99 [M–COOtBut]$^+$, 83 [M–CO$_2$–OtBut]$^+$, 57 [tBut]$^+$.

tert-Butyl-phenyl carbonate (6). Yield 99%; Rf (petroleum ether-diethylic ether 9 : 1) 0.64; δ (ppm)(300 MHz, CDCl$_3$): 1.56 (s, 9H, -OtBut), 7.08–7.44 (m, 5H, Ar) m/z = : 194 [M]$^+$, 179 [M–CH$_3$]$^+$, 94 [M–COOtBut]$^+$, 57 [tBut]$^+$.

4-Bromophenyl-*tert*-butyl carbonate (7). Yield 99%; Rf (petroleum ether-diethylic ether 9 : 1) 0.64; δ (ppm)(300 MHz, CDCl$_3$): 1.55 (s, 9H, OtBut), 7.06 (ddd, 2H, H$_C$, H$_B$, J_{orto} = 8 Hz, J_{meta} = 1.99 Hz, J_{para} = 1.80 Hz), 7.48 (ddd, 2H, H$_A$, H$_D$, J_{orto} = 8.Hz, J_{meta} = 1.99 Hz, J_{para} = 1.80 Hz); m/z: 272 [M]$^+$, 274 (90%) [M+2]$^+$·253 [M–CH$_3$]$^+$, 259 (90%) [M+2–CH$_3$]$^+$,199 [M–tBut]$^+$, 201 (90%) [M+2–tBut]$^+$. 172 [M–OtBut]$^+$, 174 (90%) [M+2–tBut]$^+$, 57 [tBut]$^+$.

tert-Butyl-4-ethylphenyl carbonate (8). Yield 99%; Rf (petroleum ether-diethylic ether 9 : 1) 0.66; δ (ppm)(300 MHz, CDCl$_3$): 1.22 (t, 3H, -CH_3CH$_2$, J_{CH3CH2} = 7.67 Hz), 1.55 (s, 9H, OtBut), 2.63 (q, 2H, -CH$_3$CH_2, J_{CH3CH2} = 7.67 Hz), 7.06 (ddd, 2H, H$_C$, H$_B$, J_{orto} = 8.Hz, J_{meta} = 1.99 Hz, J_{para} = 1.80 Hz), 7.19 (ddd, 2H, H$_A$, H$_D$, J_{orto} = 8.Hz, J_{meta} = 1.99 Hz, J_{para} = 1.80 Hz); m/z: 122 [M]$^+$, 207 [M–CH$_3$]$^+$, 122 [M–CO$_2$–isobutene]$^+$, 107 [122–CH$_3$]$^+$, 57 [tBut]$^+$.

tert-Butyl-4-nitrophenyl carbonate (9). Yield 99%; Rf (petroleum ether-diethylic ether 9 : 1) 0.46; δ (ppm)(300 MHz, CDCl$_3$): 1.58 (s, 9H, OtBut), 7.33 (ddd, 2H, H$_A$, H$_D$, J_{orto} = 8 Hz), 8.25 (ddd, 2H, H$_C$, H$_B$, J_{orto} = 8) m/z:224 [M–CH$_3$]$^+$, 176 [M–OtBut]$^+$, 139 [M–COOtBut+H]$^+$, 57 [tBut]$^+$.

Methyl-2-(*tert*-butoxycarbonylamino)-3-(4-(*tert*-butoxycarbonyloxy)phenyl)propanoate (10). Yield 99%; Rf (CH$_2$Cl$_2$–MeOH 98 : 2) 0.68; δ (ppm)(300 MHz, CDCl$_3$): 1.42 (s, 9H, NHBoc), 1.55 (s, 9H, PhOtBut), 3.00–3.150 (m, 1H, H$_1$), 3.71 (s, 3H, COOCH$_3$), 4.50–4.65 (m, 1H,H$_2$), 4.9–5.1 (m, 1H, H$_{2'}$), 7.05–7.20 (m, 4H, Ar),; m/z: 280 [M–NHBoc]$^+$, 178 [M–NHBoc–COOMe]$^+$,107 [Boc]$^+$, 57 [tBut]$^+$.

tert-Butyl-4-(2-hydroxyethyl)-2-methoxyphenyl carbonate (11a). Yield 73%; Rf (petroleum ether-diethylic ether 9 : 1) 0.60; δ (ppm)(300 MHz, CDCl$_3$): 1.55 (s, 9H, OtBut), 2.83 (t, 2H, -CH_2CH$_2$OtBut, J_{CH2CH2} = 6.59 Hz), 3.77–3.91 (m, 2H, -CH$_2$CH_2OtBut), 3.84 (s, 3H, OCH$_3$), 6.78 (dd, 1H, H$_B$, J_{orto} =

8.07 Hz, J_{meta} = 1.89 Hz), 6.82 (d, 1H, H$_C$, J_{meta} = 1.85 Hz), 7.05 (d, 1H, H$_D$, J_{orto} = 8.07 Hz); m/z: 195 [M–OtBut]$^+$, 168 [M–COOtBut–H]$^+$, 137 [M–COOtBut–OCH$_3$]$^+$.

tert-Butyl-4-(2-*tert*-butoxyethyl)-2-methoxyphenyl carbonate (11b). Yield 86%; Rf (CH$_2$Cl$_2$–MeOH 9 : 1) 0.8; δ (ppm)(300 MHz, CDCl$_3$): 1.48 (s, 9H, OtBoc), 1.55 (s, 9H, PhOtBut), 2.99 (t, 2H, -CH_2CH$_2$OtBut, J_{CH2CH2} = 7.3 Hz), 3.84 (s, 3H, OCH$_3$), 4.25 (t, 2H, -CH$_2$CH_2OPh, J_{CH2CH2} = 7.3 Hz), 6.79 (dd, 1H, H$_B$, J_{orto} = 8.07 Hz, J_{meta} = 1.89 Hz), 6.8 (d, 1H, H$_C$, J_{meta} = 1.85 Hz), 7.04 (d, 1H, H$_D$, J_{orto} = 8.07 Hz) m/z: 295 [M–OtBut]$^+$, 168 [M–2 × COOtBut]$^+$, 150 [M–2 × COOtBut–2 × CO$_2$]$^+$,137 [M–2 × COOtBut–OCH$_3$]$^+$.

tert-Butyl 2-methoxyphenyl carbonate (12). Yield 98%; Rf (Petroleum Ether-Diethylic Ether 9 : 1) 0.38; δ (ppm)(300 MHz, CDCl$_3$): 1.55 (s, 9H, OtBut), 3.85 (s, 3H, -OCH$_3$), 6.90–7.19 (m, 4H, Ar); m/z: 224 [M]$^+$, 151[M–OtBut]$^+$, 124 [M–COOtBut]$^+$, 109 [M–OCOOtBut]$^+$, 92 [M–OCOOtBut–CH$_3$]$^+$, 77 [Ph]$^+$.

tert-Butyl 4-methylphenyl carbonate (13). Yield 99%; Rf (petroleum ether-diethylic ether 9 : 1) 0.7; δ (ppm)(300 MHz, CDCl$_3$): 1.55 (s, 9H, OtBut), 2.33 (s, 3H, -CH$_3$), 7.04 (ddd, 2H, H$_C$, H$_B$, J_{orto} = 7.30 Hz, J_{meta} = 3.01 Hz, J_{para} = 1.00 Hz), 7.15 (ddd, 2H, H$_A$, H$_D$, J_{orto} = 7.30 Hz, J_{meta} = 3.01 Hz, J_{para} = 1.00 Hz); m/z: 208 [M]$^+$, 193 [M–CH$_3$]$^+$, 108 [M–CO$_2$–isobutene]$^+$, 91 [M–COOtBut]$^+$, 77 [Ph]$^+$.

tert-Butyl 2-methylphenyl carbonate (14). Yield 97%; Rf (petroleum ether-diethylic ether 9 : 1) 0.7; δ (ppm)(300 MHz, CDCl$_3$): 1.55 (s, 9H, OtBut), 2.33 (s, 3H, -CH$_3$), 7.06–7.22 (m, 4H, Ar); m/z: 208 [M]$^+$, 193 [M–CH$_3$]$^+$, 108 [M–CO$_2$–isobutene]$^+$, 91 [M–COOtBut]$^+$, 77 [Ph]$^+$.

Cleavage of *tert*-butyl carbonates

Oil bath heating cleavage of *tert*-butyl carbonates. In a general procedure 1.0 mmol of *tert*-butyl ether was solved in 2.0 ml of EtOH and, after addition of 5% mol of Er (OTf)$_3$ (0.50 mmol, 30.70 mg), the mixture was heated until reflux temperature (70 °C) in an oil bath. The reaction was monitored by TLC or GC-MS. On completion, the mixture was diluted with ether, then extracted for three times with water. The organic phases collected were dried on Na$_2$SO$_4$, filtered and then evaporated under vacuum giving rise to the pure product.

MW-assisted cleavage of *tert*-butyl carbonates. In a general procedure 1.0 mmol of *tert*-butyl ether was solved in 2.0 ml of EtOH and 1% mol of Er (OTf)$_3$ (0.O10 mmol, 6.140 mg) were added in a 0.3–3 ml glass vials from Anton Paar sealed with a dedicated PEEK screw-cup together with a reliable PTFE seal. The mixture was reacted for 25 min in a Synthos 3000 instrument from Anton Paar, equipped with a 64MG5 rotor and an IR probe as external control of the temperature, fixed on the temperature value of 80 °C. On completion, the mixture was diluted with ether, then extracted for three times with water. The organic phases collected were dried on Na$_2$SO$_4$, filtered and then evaporated under vacuum giving rise to the pure product.

Notes and references

1 P. T. Anastas and J. C. Warner, in *Green Chemistry: Theory and Practice*, Oxford University Press, 1988; P. Tundo, P. Anastas, D. St, C. Black, J. Breen, T. Collins, S. Memoli, J. Miyamoto, M. Polyakoff and W. Tumas, *Pure Appl. Chem.*, 2000, **72**, 1207–1403.

2 A. S. Matlack, in *Introduction to Green Chemistry*, Marcel Dekker Inc., New York, 2001; M. Lancester, in *Green Chemistry: An Introductory Text*, Royal Society of Chemistry, Cambridge, 2002; J. H. Clark and D. Macquarrie, in *Handbook of Green Chemistry & Technology*, Blackwell Publishers, Oxford, 2002.

3 *Microwave-Assisted Organic Synthesis*, ed., P. Lidstrçm and J. P. Tierney, Blackwell Publishing, Oxford, 2005; C. O. Kappe and A. Stadler, in *Microwaves in Organic and Medicinal Chemistry*, Wiley-VCH, Weinheim, 2005; A. Loupy, in *Microwaves in Organic Synthesis* 2nd ed., Wiley-VCH, Weinheim, 2006; M. Larhed and K. Olofsson, in *Microwave Methods in Organic Synthesis*, Springer, Berlin, 2006; C. O. Kappe, *Angew. Chem.*, 2004, **116**, 6408–6443, (*Angew. Chem., Int. Ed.*, 2004, **43**, 6250); B. L. Hayes, *Aldrichimica Acta*, 2004, **37**, 66–77.

4 G. Cravotto and P. Cintas, *Chem. Soc. Rev.*, 2006, 180–196; G. Cravotto and P. Cintas, *Angew. Chem.*, 2007, **119**, 5573–5575, (*Angew. Chem., Int. Ed.*, 2007, **46**, 5476).

5 U. M. Lindstrom, in *Organic Reactions in Water*, Blackwell, Oxford, UK, 2007; C. J. Li, *Chem. Rev.*, 2005, **105**, 3095–3165; U. M. Lindström, *Chem. Rev.*, 2002, **102**, 2751–2772; S. Minakata and M. Komatsu, *Chem. Rev.*, 2009, **109**, 711–724; D. Dallinger and C. O. Kappe, *Chem. Rev.*, 2007, **107**, 2563–2591.

6 K. Tanaka, in *Solvent-free Organic Synthesis*, Wiley-VHC, 2003; R. S. Varma, *Green Chem.*, 1999, **1**, 43–55.

7 A. A. G. Shaikh and S. Sivaram, *Chem. Rev.*, 1996, **96**, 951–976; J. P. Parrish, R. N. Salvatore and K. W. Jung, *Tetrahedron*, 2000, **56**, 8207–8237.

8 T. W. Greene and P. G. M. Wuts, in *Protecting Groups in Organic Synthesis*, 4th ed., Wiley & Sons, New York, 2007; P. J. Kocienski, in *Protecting Groups*, 3rd ed., Georg Thieme Verlag, New York, 2004; A. F. Hegarty, in *Comprehensive Organic Chemistry*, Vol. **2**, Sutherland, I. O., Pergamon, London, 1979, 1067.

9 Some selected references follow: B. Veldurthy, J. M. Clacens and F. Figueras, *Eur. J. Org. Chem.*, 2005, **10**, 1972–1976; P. Tundo, L. Rossi and A. Loris, *J. Org. Chem.*, 2005, **70**, 2219–2224; R. Srivastava, D. Srinivasa and P. Ratnasamy, *Appl. Catal., A*, 2005, **289**, 128–134; B. Veldurthy and F. Figueras, *Chem. Commun.*, 2004, **10**, 734–735; M. O. Bratt and P. Taylor, *J. Org. Chem.*, 2003, **68**, 5439–5444; S. Carloni, D. De Vos, P. A. Jacobs, R. Maggi, G Sartori and R. Sartorio, *J. Catal.*, 2002, **205**, 199–204; M. Verdecchia, M. Feroci, L. Palombi and L. Rossi, *J. Org. Chem.*, 2002, **67**, 8287–8289; P. Tundo and M. Selva, *Acc. Chem. Res.*, 2002, **35**, 706–716; R. N. Salvatore, F. Chu, A. S Nagle, E. A. Kapxhiu, R. M. Cross and K. W. Jung, *Tetrahedron*, 2002, **58**, 3329–3347; J. S. Savita and R. V. Jayaram, *Tetrahedron Lett.*, 2008, **49**, 4249–4251.

10 D. K. Mohapatra, *Synlett*, 2001, 1995–1996; F. Houlihan, F. Bouchard, J. M. J. Frechet and C. G. Willson, *Can. J. Chem.*, 1985, **63**, 153–162; Y. Basel and A. J. Hassner, *J. Org. Chem.*, 2000, **65**, 6368–6380; M. M. Hansen and J. R. Riggs, *Tetrahedron Lett.*, 1998, **39**, 2705–2706; G. Bartoli, M. Bosco, A. Carlone, R. Dalpozzo, M. Locatelli, P. Melchiorre, P. Palazzi and L. Sambri, *Synlett*, 2006, 2104–2108; C. T. Chen, J. H. Kuo, V. D. Pawar, Y. S. Munot, S. S. Weng, C. H. Ku and C. Y. Liu, *J. Org. Chem.*, 2005, **70**, 1188–1197; C. T. Chen, J. H. Kuo, C. H. Li, N. B. Barhate, S. W. Hon, T. W. Li, S. D. Chao, C. C. Liu, Y. C. Li, I. H. Chang, J. S. Lin, C. J. Liu and Y. C. Chou, *Org. Lett.*, 2001, **3**, 3729–3732.

11 R. Dalpozzo, A. De Nino, L. Maiuolo, A Procopio, A. Tagarelli, G. Sindona and G. Bartoli, *J. Org. Chem.*, 2002, **67**, 9096–9098; G. Bartoli, R. Dalpozzo, A. De Nino, L. Maiuolo, M. Nardi, A. Procopio and Antonio Tagarelli, *Green Chem.*, 2004, **6**, 191–192; A. Procopio, R. Dalpozzo, A. De Nino, L. Maiuolo, B. Russo and G. Sindona, *Adv. Synth. Catal.*, 2004, **346**, 1465–1470; A. Procopio, R. Dalpozzo, A. De Nino, L. Maiuolo, M. Nardi and B. Russo, *Adv. Synth. Catal.*, 2005, **347**, 1447–1450; A. Procopio, R. Dalpozzo, A. De Nino, L. Maiuolo, M. Nardi and G. Romeo, *Org. Biomol. Chem.*, 2005, **3**, 4129–4133; A. Procopio, M. Dal Pozzo, A. De Nino, L. Maiuolo, M. Oliverio, B. Russo and A. Tocci, *Aust. J. Chem.*, 2007, **60**, 75–79; A. Procopio, M. Gaspari, M. Nardi, M. Oliverio and R. Romeo, *Tetrahedron Lett.*, 2008, **49**, 1961–1964.

12 (*a*) A. Procopio, G. Das, M. Nardi, M. Oliverio and L. Pasqua, *ChemSusChem*, 2008, **1**, 916–919; (*b*) A. Procopio, G. De Luca, M. Nardi, M. Oliverio and R. Paonessa, *Green Chem.*, 2009, **11**, 770–773.

13 G. Bartoli, M. Bosco, A. Carlone, R. Dalpozzo, M. Locatelli, P. Melchiorre and L. Sambri, *J. Org. Chem.*, 2006, **71**, 9580–9588.

14 B. M. Pope, S.-J. Sheu, R. L. Stanley, D. S. Tarbell and Y. Yamamoto, *J. Org. Chem.*, 1978, **43**, 2410–2414; C. S. Dean, D. S. Tarbell and A. W. Friederang, *J. Org. Chem.*, 1970, **35**, 3393–3397.

15 Y. Kegelaers, O. Eulaerts, J. Reisse and N. Segebarth, *Eur. J. Org. Chem.*, 2001, **19**, 3683–3688; G. Cravotto and P. Cintas, *Chem. Soc. Rev.*, 2006, **35**, 180–196.

16 For a survey of microwave instrument software, see: C. O. Kappe, D. Dallinger and S. S. Murphree, in *Practical Microwave Synthesis for Organic Chemists - Strategies Instruments and Protocols*, Wiley-VCH, Weinheim, 2009, ch. 5, pp 172–173.