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A convenient synthesis of *tert*-butyl ethers under microwave condition

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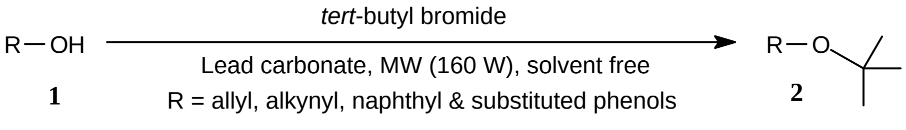
Synthesis of *tert*-butyl ethers from various alcohols and substituted phenols can be achieved using *tert*-butyl bromide in the presence of basic lead carbonate as a catalyst under microwave irradiation in absence of solvent. The catalyst is easily recovered *via* filtration and reused up to three times without appreciable loss of activity.

Keywords: Lead carbonate, microwave irradiations, *tert*-butyl ethers, *tert*-butyl bromide, phenol

The protection of alcohols as *tert*-butyl ethers has become a widely utilized procedure in organic synthesis[1]. The *tert*-butyl ether in fact is one of the most under used alcohol protecting groups, although it is stable under strongly basic condition and can be cleaved with relative ease under acidic conditions[2]. The chemical synthesis of *tert*-butyl ethers are well documented in the literature[1,2]. Some of the common procedures involve the exposure of the alcoholic or phenolic species to excess of isobutylene in the presence of acid catalysts such as borontrifluride-phosphoric acid complex or sulfuric acid at 0-25°C (ref. 3) or trifluromethane sulfonic acid in dichloromethane at –50°C (ref. 4). In some examples non acidic conditions like the reaction of *tert*-butanol and alkanol using anhydrous magnesium sulfate are employed to synthesize *tert*-butyl alkyl ethers. This method is useful for the synthesis of *tert*-butyl esters as well[5]. Other methods include Pd/P(t-Bu)$_3$ catalyzed reactions of aryl halides with sodium *tert*-butoxide for the synthesis of aryl *tert*-butyl ethers[6] and magnesium perchlorate catalysed reaction of alcohol with *tert*-butyldicarbonate to get alkyl and aryl *tert*-butyl ethers[7]. Most of these protocols either require longer reaction time or critical reaction conditions such as reaction of low boiling isobutylene under autoclave conditions. Further, these protocols usually require chromatographic separations for obtaining pure products. Herein is reported a novel method which works within a couple of seconds under microwave conditions as shown in **Scheme I**. The products are normally obtained in a pure form by solvent trituration and filtration.

Results and Discussion

In this paper is reported a simple and efficient etherification of allyl and alkynyl alcohols, and substituted phenols which easily reacted with *tert*-butyl bromide in the presence of lead carbonate heated under microwave irradiation (160W) at 85-89°C under solvent free conditions with good to excellent yields of respective *tert*-butyl ethers within 60-80 sec. The results are summarized in **Table I**. The same process was successfully extended to get other *tert*-butyl ether derivatives, for example (entry 10, **Table II**) 3-hyroxy-benzyl alcohol (10 mmol) reacted with *tert*-butyl bromide (40 mmol) in the presence of lead carbonate (2 mmol), at 92°C over 200 sec to result in the formation of the corresponding product 1-*tert*-butyl-3-(*tert*-butoxymethyl) benzene in 88% yield. Similarly, the allyl and alkynyl alcohols, 1-pentanol and 1-octanol (entry 1-4, **Table II**) reacted



Scheme I

Table I — Reaction of phenol with *tert*-butyl bromide under various conditions[a] in the presence of $2PbCO_3Pb(OH)_2$.

Entry	Amount of *t*-BuBr (mmol)	$2PbCO_3Pb(OH)_2$ (mmol)	Time (sec)	Temp (°C)[e]	Yield[b] (%)
1	20	1	60	85	>90
2	10	1	180	90	55(45)[c]
3	20	2	200	95	90
4	10	2	250	105	<50
5	15	2	250	110	65
6	20	1(3)[d]	80	98	90(85%)[d]
7	40	-	360	150	<25

[a] Reaction condition: Phenol (10 mmol), *t*-BuBr, $2PbCO_3Pb(OH)_2$, temperature and time as shown in table,

[b] Isolated product, [c] Recovered phenol, [d] Run with recycled lead carbonate obtained by washing with ethyl acetate, dried and reused, [e] After irradiations of reaction mass insert the thermometer

smoothly with *tert*-butyl bromide, in the presence of lead carbonate to afford 85, 86, 80 and 82% of 3-*tert*-butoxyprop-1-ene, *tert*-butylprop-2-ynyl ether, *tert*-butyl pentyl ether and *tert*-butyl octyl ether respectively.

Recovery of the catalyst was accomplished by simple filtration or by centrifugation followed by washing with ethyl acetate. Notably, the reactions gave excellent results with a various substituted phenols (entry 5-8); α- and β-naphthol (entries 11 and 12) they can be converted into the corresponding *tert*-butyl ethers in high yields, without any detectable side products arising from an electrophilic substitution on the aromatic ring. The reaction is highly chemo-selective. In fact, other functionalities present in the phenols such as methoxy, chloro and fluro groups survived under the reaction conditions adopted.

Experimental Section

NMR spectrum was recorded on 300 MHz and 400 MHz Brucker spectrometer. All chemicals were of commercial grade and used as received except 3-hydroxy benzyl alcohol which was synthesized in-house from 3-hydroxybenzaldehyde according to the procedure mentioned in the literature[8].

General procedure for the synthesis of *tert*-butyl ethers

To a mixture of phenol (10 mmol) and lead carbonate (1 mmol) taken in a 50 mL sealed tube cooled to 0°C, was added *tert*-butyl bromide (20 mmol) dropwise. The mixture was placed in microwave oven and irradiated at 85°C for the given period of time (**Table II**). After completion of the reaction, the mixture was cooled to RT, EtOAc (2×10 mL) was added to the reaction mixture, stirred for a while and filtered. The filtrate was washed with 10% NaOH followed by saturated brine solution, dried over anhydrous Na_2SO_4 and concentrated on a rotavapor to afford pure *tert*-butoxybenzene (entry 4, **Table II**, compound **2e**) in 90% yield. All products were characterized by NMR spectral analysis.

In conclusion, a novel general and convenient method for the synthesis of *tert*-butyl ethers under microwave condition has been developed.

Characterization Data

3-*tert*-Butyl prop-1-ene, 2a: ^{1}H NMR ($CDCl_3$): δ 1.2 (s, 9H), 3.90-3.92 (d, 2H), 5.10-5.11 (d, 1H), 5.13-5.14 (d, 1H), 5.8-5.9 (m,1H); ^{13}C NMR ($CDCl_3$): δ 27.5(CH_3), 63.05 (OCH_2), 73.6(C), 115.6 (C), 136.2(C).

***t*-Butyl prop-2-ynyl ether, 2b**: ^{1}H NMR ($CDCl_3$): δ 1.25 (s, 9H), 2.4 (S, 1H), 4.1 (S, 2H); ^{13}C NMR ($CDCl_3$): δ 27.3(CH_3), 31.0 (CH), 36.3(C), 53.24 (C), 72.82(C).

***t*-Butyl pentyl ether**, **2c**: ^{1}H NMR ($CDCl_3$): δ 0.76 (t, 3H), 1.2 (s, 9H)1.25 (m, 2H), 1.36 (m,2H), 1.57(m,2H), 3.56(m,2H); ^{13}C NMR ($CDCl_3$):δ 14.0(CH_3), 22.7(CH_3), 28.3(CH_2), 29.2 (CH_2), 32.0 (CH_2), 62.0 (OCH_2), 71.9(C).

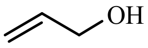
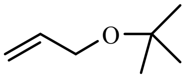
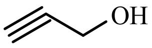
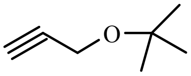
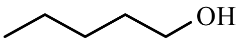
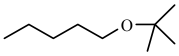
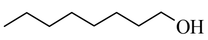
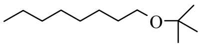
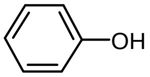
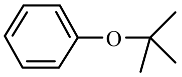
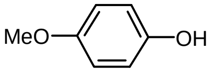
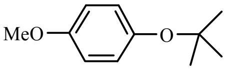
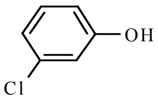
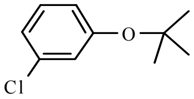
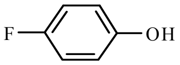
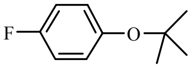
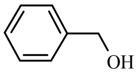
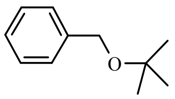
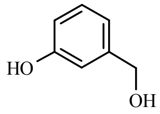
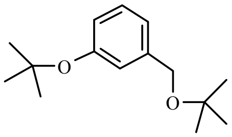
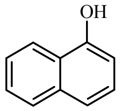
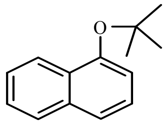
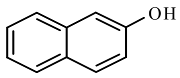
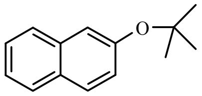
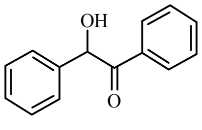
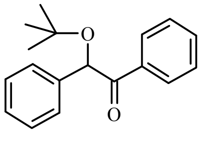
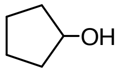
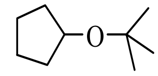
1-*t*-Butoxyoctane, 2d (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 0.88 (t, J = 6.8, 3H), 1.19 (s, 9H), 1.20-1.40 (m, 10H), 1.45-1.55 (m, 2H), 3.32 (t, J=6.6, 2H); ^{13}C NMR ($CDCl_3$): δ 14.0(CH_3), 22.6 (CH_2), 26.2(CH_2), 27.5 (CH_3), 29.3(CH_2), 29.5 (CH_2), 30.7(CH_2), 31.8 (CH_2), 61.6 (CH_2), 72.3(C).

1-*t*-Butoxybenzene, 2e (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 1.35 (s, 9H), 6.95-7.00 (m, 2H), 7.05-7.10 (m, 1H), 7.25-7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 29.4 (CH_3), 78.3 (C), 123.3 (CH), 124.2 (CH), 128.8 (CH), 131.9 (C).

1-*t*-Butoxy-4-methoxybenzene, 2f (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 1.33 (s, 9H), 3.72 (s, 3H), 6.76(m, 4H); ^{13}C NMR ($CDCl_3$): δ 28.0(CH_3), 56 (C), 71.7, 78.0 (C), 113.8 (CH),123.5 (C), 154.3(C).

1-*t*-Butoxy-3-chlorobenzene, 2g (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 1.35 (s, 9H), 6.88 (dd, 1H), 7.00 (t, 1H), 7.05 (dd, 1H), 7.18 (t, 1H); ^{13}C NMR ($CDCl_3$): δ 28.8 (CH_3), 79.2 (C), 122.2 (CH), 123.4 (CH), 124.3 (CH), 129.6 (CH), 134.0 (C), 156.4 (C).

Table II — Synthesis of *tert*-butyl ethers under mild conditions

Entry	Substrate	Time(sec)	Product[a]		Temp (°C)	Yield(%)[b]
1		80		**2a**	92	85
2		80		**2b**	92	86
3		60		**2c**	85	80
4		60		**2d**	88	82
5		60		**2e**	85	90
6		80		**2f**	94	92
7		80		**2g**	95	88
8		80		**2h**	89	82
9		120		**2i**	110	96
10		200		**2j**	92	88
11		90		**2k**	105	75
12		90		**2l**	108	86
13		90		**2m**	106	82
14		96		**2n**	110	84

[a] All products are known except **2a**, **2b**, **2c** and **2j** which are novel and characterized by NMR spectral analysis,
[b] Isolated yields.

1-*t*-Butoxy-4-fluorobenzene, 2h (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 1.31 (s, 9H), 6.93 (s, 2H), 6.94(s, 2H); ^{13}C NMR ($CDCl_3$): δ 28.7(CH_3), 78.5 (C), 115.2 (d, CH), 125.5 (d, CH), 151.1(C), 159.1(d, C).

1-(*t*-Butoxymethyl)benzene, 2i (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 1.31 (s, 9H), 4.47 (s, 2H), 7.25-7.40 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 27.7 (CH_3), 64.1 (CH_2), 73.4 (C), 127.1 (CH), 127.4 (CH), 128.3 (CH), 139.9 (C).

1-*t*-Butoxy-3-(tert-butoxymethyl)benzene, 2j: ^{1}H NMR ($CDCl_3$): δ 1.29 (s, 9H), 1.35 (S, 9H), 4.42 (S, 2H), 6.8 (d, 1H), 6.9 (s,1H), 7.0 (d, 1H), 7.3(m, 1H); ^{13}C NMR ($CDCl_3$): δ 27.6(CH_3), 28.8 (CH), 63.8 (OCH_2), 73.3 (C), 77.9(C), 113.7 (C), 116.7 (C), 119.8 (C), 128.5(CH), 141.0(CH), 158.8 (CH).

1-*t*-Butoxynaphthalene, 2k (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 1.46 (s, 9H), 7.10 (dd, 1H), 7.33(t, 1H), 7.40-7.45 (m, 2H), 7.50 (d, 1H), 7.75-7.80 (m, 1H), 8.20-8.25(m,1H); ^{13}C NMR ($CDCl_3$): δ 29.1(CH_3), 79.7(C), 116.3(CH), 122.3(CH), 123.4(CH), 125.1(CH), 125.4(CH), 125.9(CH), 127.5 (CH), 130.0(C), 134.8(C), 152.1(C).

2-*t*-Butoxynaphthalene, 2l (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 1.41 (s, 9H), 7.18 (dd, 1H), 7.35-7.45(m, 3H), 7.65-7.80 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 28.9 (CH_3), 78.9 (C), 119.7 (CH), 124.4 (CH), 125.0 (CH), 125.9 (CH), 127.2 (CH), 127.9 (CH), 128.5 (CH), 130.3 (C), 134.1 (C), 152.1 (C).

2-*t*-Butoxy-1,2-diphenylethanone, 2m (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 1.25 (s, 9H), 5.62 (s, 1H), 7.20-7.55 (m, 8H), 8.05-8.10 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 28.0 (CH_3), 76.0 (C), 79.7 (CH), 126.1 (CH), 127.6 (CH), 128.1 (CH), 128.5 (CH), 130.0 (CH), 132.7 (CH), 135.2 (C), 138.6 (C), 200.1 (C).

***t*-Butoxycyclopentane 2n** (Ref. 7): ^{1}H NMR ($CDCl_3$): δ 1.18 (s, 9H), 1.40-1.50 (m, 4H), 1.60-1.85(m, 4H), 3.95-4.05 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 23.7 (CH_2), 28.6 (CH_3), 34.9 (CH_2), 72.8 (CH), 73.5 (C).

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