

A high yielding, one-pot synthesis of dialkyl carbonates from alcohols using Mitsunobu's reagent

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This Letter is dedicated to Dr. Suprabhat Ray on the occasion of his 65th birthday

Abstract—A Mitsunobu-based protocol has been developed for the synthesis of symmetrical and unsymmetrical dialkylcarbonates from a variety of primary, secondary and tertiary alcohols using gaseous carbon dioxide, in good to excellent yields. This protocol is mild and efficient compared to other reported methods.

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Organic carbonates constitute an important and versatile class of compounds for a variety of industrial, synthetic and medicinal applications.¹ They have been used extensively as pharmaceuticals,² agrochemicals³ and intermediates in organic synthesis,⁴ for protection of hydroxy groups⁵ and as linkers in combinatorial chemistry.⁶ Moreover, their use as efficient solvents,⁷ in polymer chemistry⁸ for the synthesis of polycarbonates and in many industrial applications⁹ are well known. These uses require their preparation by convenient and safe methodology. Classical syntheses of carbonates involve the use of phosgene,¹⁰ its derivatives¹¹ or carbon monoxide.¹² These methods have associated drawbacks such as the use of costly, toxic and corrosive reagents. Recently, the replacement of phosgene with carbon dioxide¹³ in the synthesis of carbonates starting from hydroxy compounds has been proposed by several authors. Carbon dioxide has been utilized gaseous,¹⁴ electrochemically,¹⁵ supercritically¹⁶ and in combination with metals and non metals.¹⁷ However, most of these methods suffer from limitations such as long reaction times, use of expensive strongly basic reagents, tedious work-up and low yields. Consequently, there is continued interest in developing new and convenient methods

for the synthesis of dialkylcarbonates using mild reaction conditions.

Our group¹⁸ has been engaged over several years on the development of new methods for the synthesis of carbamates and dithiocarbamates using CO₂ and CS₂. Recently, we reported¹⁹ the synthesis of carbamates, dithiocarbamates and *O,S*-dialkyl dithiocarbonates (xanthates) from the corresponding alcohols using Mitsunobu's reagent. Based on our recent work,¹⁸ we report herein a chemoselective, highly efficient and mild synthesis of dialkyl carbonates of primary, secondary and tertiary alcohols using Mitsunobu's reagent.

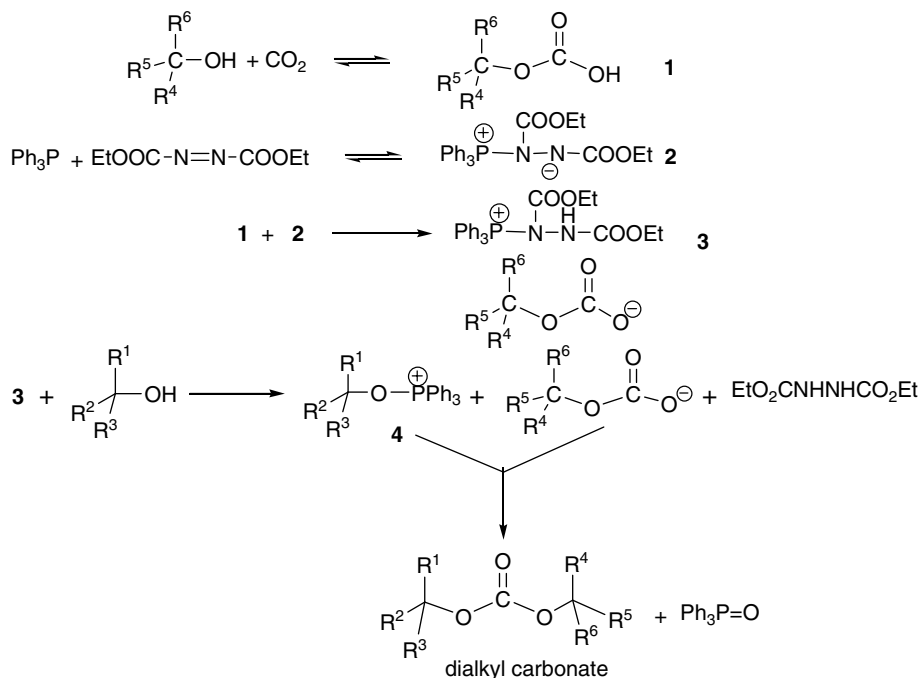
Thus we carried out¹⁹ the synthesis of carbonates by mild carbonation of alcohols with gaseous carbon dioxide and a second alcohol in the presence of Mitsunobu's reagent. Since the reactivity of CO₂ is less than CS₂, a reaction temperature of 90–100 °C was used.

We assume that the unstable carbonic acid **1** generated from an alcohol and CO₂ reacts with the Mitsunobu zwitterion **2** formed from Ph₃P and diethyl azodicarboxylate, to furnish the stabilized zwitterionic species **3** which in turn undergoes *O*-alkylation giving rise to the formation of the carbonate ester as shown in [Scheme 1](#).

Thus, various alcohols were reacted using Mitsunobu's reagent and gaseous carbon dioxide in dry dimethylsulfoxide (DMSO) at 90–100 °C for 4–8 h, to afford dialkyl

Keywords: Mitsunobu's reagent; Carbon dioxide; Alcohols; Dialkylcarbonates; Carbonation.

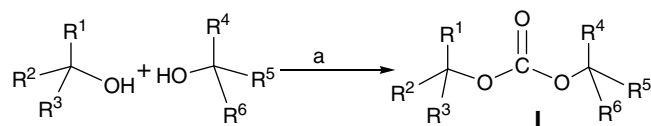
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Scheme 1. Proposed mechanism of formation of dialkyl carbonates.

carbonates²⁰ in good to excellent yields (70–98%) as shown in Table 1. We examined several solvents such as *n*-heptane, *n*-hexane, DMSO, DMF and HMPA of which dry DMSO proved to be the most suitable. The overall reaction is shown in Scheme 2.

In conclusion, we have developed a convenient and efficient protocol for the one-pot coupling of various alcohols with a variety of primary, secondary and tertiary alcohols via a Mitsunobu zwitterion. This reaction generates the corresponding, dialkyl carbonates in high yields. Furthermore, this method exhibits substrate ver-



Scheme 2. Reagents and conditions: (a) dry DMSO, DEAD/Ph₃P, CO₂, 90–100 °C, 4–8 h.

satility, mild reaction conditions and experimental convenience. This synthetic protocol is believed to offer a more general method for the formation of C–O bonds.

Table 1. Conversion of alcohols into carbonates of general formula **I**^a

Entry	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	Time (h)	Isolated yield (%)
1	Phenyl	H	H	Phenyl	H	H	5	90
2	2-Phenethyl	H	H	<i>n</i> -Hexyl	H	H	4	96
3	2-Phenethyl	H	H	<i>n</i> -Propyl	<i>n</i> -Propyl	H	5	85
4	<i>n</i> -Propyl	H	H	<i>n</i> -Octyl	H	H	5	91
5	<i>i</i> -Amyl	H	H	Cyclohexyl	H	H	6	84
6	<i>n</i> -Butyl	H	H	<i>n</i> -Butyl	H	H	5	82
7	2-Naphthyloxyethyl	H	H	Phenyl	H	H	6	80
8	2-Naphthyloxyethyl	H	H	4-Methoxyphenyl	H	H	5	83
9	<i>n</i> -Butyl	<i>n</i> -Butyl	H	<i>n</i> -Octyl	H	H	6	81
10	<i>n</i> -Butyl	<i>n</i> -Butyl	<i>n</i> -Butyl	<i>n</i> -Dodecyl	H	H	7	75
11	<i>n</i> -Hexyl	H	H	Phenyl	H	H	6	78
12	<i>n</i> -Heptyl	H	H	Benzyl	H	H	5	82
13	<i>n</i> -Octyl	H	H	3-Methoxybenzyl	H	H	5	88
14	<i>n</i> -Heptyl	H	H	<i>n</i> -Dodecyl	H	H	4	98
15	<i>n</i> -Pentyl	Methyl	H	Cyclohexyl	H	H	6	90
16	2-Naphthyloxyethyl	H	H	<i>n</i> -Butyl	<i>n</i> -Butyl	<i>n</i> -Butyl	8	70
17	3-(2-Naphthyloxy)prop-1-yl	H	H	<i>n</i> -Octyl	H	H	5	90
18	<i>n</i> -Heptyl	H	H	2-Phenethyl	H	H	4	96
19	<i>n</i> -Decyl	H	H	<i>n</i> -Butyl	<i>n</i> -Butyl	<i>n</i> -Butyl	6	78

^a All the products were characterized by IR, NMR and mass spectral data.

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- Typical experimental procedure: Dibenzyl carbonate (entry 1): Benzyl alcohol (1 ml, 9 mmol) was taken in dry DMSO (35 ml) and gaseous CO₂ was bubbled through it for 30 min. To this, a mixture of triphenylphosphine (2.2 g, 9 mmol) and diethyl azodicarboxylate (1.33 ml, 9 mmol) was added slowly in 2–3 small portions. Next, benzyl alcohol (1 ml, 9 mmol) was added. The reaction was stirred until completion (5 h) as confirmed by TLC. The reaction mixture was then poured into distilled water (50 ml) and extracted with ethyl acetate thrice. The organic layer was separated and dried over anhydrous sodium sulphate and then concentrated to afford dibenzyl carbonate as an oil (2.06 g, 90%). IR (neat): 1750 (C=O) cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.55 (s, 4H, J = 7.2 Hz, PhCH₂O), 7.22–7.41 (m, 10H, Ar-H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ = 74.5 (PhCH₂O), 127.5, 128.5, 129.6, 131, 140.10, 142.20 (aromatic region), 158.5 (C=O) ppm; Mass (EIMS): m/e (%) = 243 (M+H⁺, 89%), 152 (42), 91(100); Anal. Calcd for C₁₅H₁₄O₃: C, 74.36; H, 5.82. Found: C, 74.56; H, 5.61.