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Activation of Benzyl Aryl Carbonates: The Role of Cation−π Interactions

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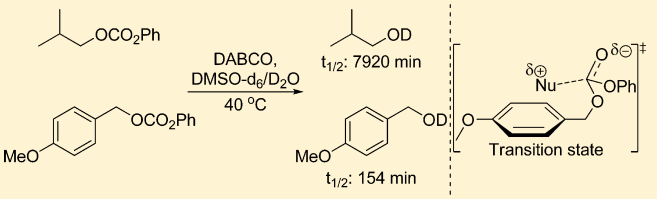
Supporting Information

ABSTRACT: Benzyl aryl carbonates can react with a nucleophile to yield an activated electrophile and an aryloxide anion. Previously, we had utilized this in the synthesis of α-nitro esters from nitroalkanes. To further understand the process of activation of these carbonates by nucleophiles, we have performed kinetic studies on the hydrolysis of carbonates using nucleophiles. Rate constants for the hydrolysis were obtained under pseudo-first-order conditions with DABCO as the nucleophile. A comparison of rate constant for hydrolysis of isobutyl phenyl carbonate with benzyl phenyl carbonate shows that the presence of benzyl group results in a 16-fold acceleration of hydrolysis rate. This indicates that the transition state for activation of carbonate is stabilized by cation−π interactions. A comparison of the rate constant for various aromatic rings indicates that electron-donating substituents on the benzyl groups accelerate the rate of hydrolysis. Studies were also carried out with DMAP as nucleophile and the results are presented. Our studies show that stable carbonates can be activated using nucleophiles. Activated acyl groups generated from acid anhydrides have been used in several enantioselective reactions. Our studies show that carbonates can be stable alternatives to acid anhydrides.

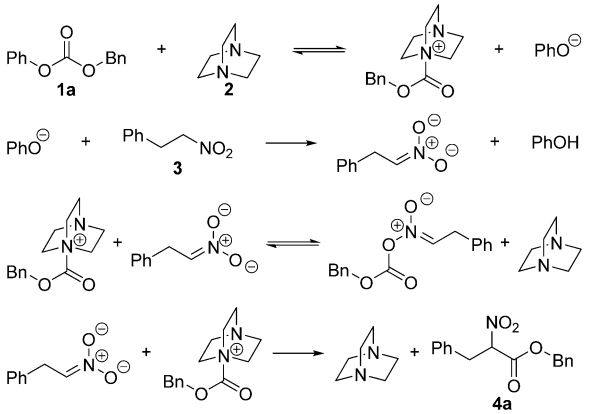


INTRODUCTION

The Strecker reaction is one of the most versatile methods for the synthesis of α-amino acids.[1] Although the utility of this method is well established, the toxicity of cyanide is a major concern with this reaction. In an attempt to develop a more benign reaction, we reported on the use of carbonate as a carboxyl group synthon in the synthesis of α-nitro esters (Scheme 1).[2]

In this method, benzyl phenyl carbonate is activated with DABCO to transiently generate an activated electrophile and phenoxide. Deprotonation of a nitroalkane by the phenoxide generates a nitronate anion. Reaction of nitronate anion with the activated electrophile through oxygen atom is rendered reversible by DABCO, while attack through carbon leads to the formation of an α-nitro ester.[2−4]

Scheme 1. Synthesis of α-Nitro Esters Using Carbonates as Carboxyl-Group Equivalents



The nucleophilic activation of carbonates generates an activated acyl group. Smith and co-workers have shown that nucleophilic activation of carbonates can be used for an *O*- to *C*-carboxyl transfer.[5] Initial reports focused on the use of a N-Heterocyclic carbene as nucleophile. Later, an enantioselective version was reported using a chiral isothiourea.[6] Recently, Lou and co-workers have shown that carbonates can be used to trap the product of reaction between glycine imine esters and aryl aldehydes.[7] The aldol products are difficult to isolate as the reactions are reversible.[8] Trapping the hydroxyl group with carbonate facilitates isolation of aldol products, which are then readily converted to β-hydroxy-α-amino acids. The generation of an activated acyl group from a stable carbonate under mild conditions is likely to be useful in similar applications. To understand this fundamental step, we have studied the hydrolysis of various carbonates in the presence of nucleophiles (Figure 1). Our studies indicate a likely role for cation−π interactions in the activation of carbonates. Cation−π interactions have been shown to play a key role in stabilizing protein structures[9] and in stabilizing transition states of

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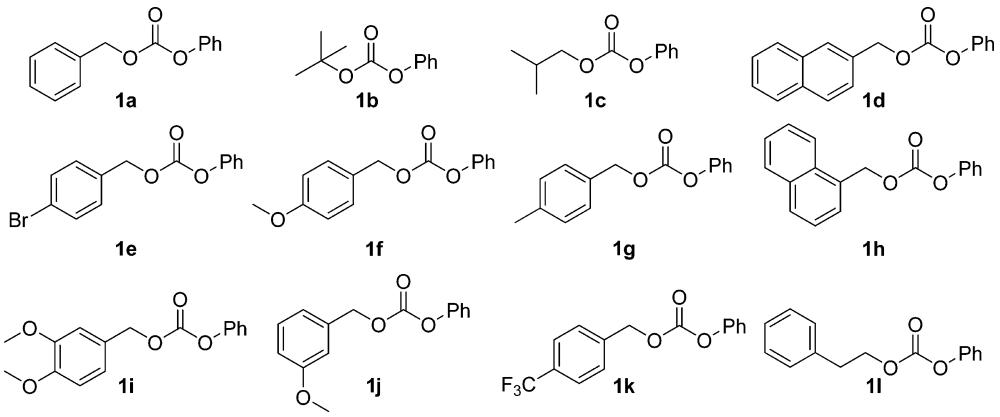


Figure 1. Structure of carbonates used in this study.

enzymatic[10] as well as nonenzymatic reactions.[11] Additionally, cation−π interactions have also been invoked as key factors in enhancing the enantioselectivity of several organo-catalyzed reactions.[12] Herein, we report kinetic studies on the activation of carbonates that support our hypothesis.

RESULTS AND DISCUSSION

As mentioned earlier, we had developed a synthesis of α-nitro esters using benzyl phenyl carbonate as the source of carboxyl group. To further extend the scope of our reaction, we explored combinations of several solvents and carbonates. In this context, a reaction was performed with t-butyl phenyl carbonate (**1b**), 2-phenyl nitroethane, and DABCO using EtOAc as the solvent. Under these conditions, we failed to observe any product formation and the starting materials were recovered in good yield (Table 1). To test whether this was due to steric

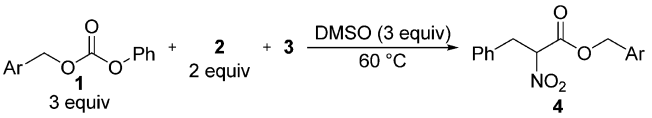
Table 1. Formation of α-Nitro Esters with Various Carbonates

entry	carbonate	% yield	% nitro alkane recovered	% carbonate recovered
1	**1b**	0	85	>95
2	**1c**	0	86	>95
3	**1a**	64	0	0

crowding, the less hindered isobutyl phenyl carbonate (**1c**) was evaluated under the same conditions. Here again, we could not obtain any product and the starting materials were recovered. When benzyl phenyl carbonate was used under the same conditions, the product was obtained in 64% yield. These experiments indicated a key role for the benzyl group in activation of the carbonate.

In order to clarify the role of benzyl groups in this reaction, we evaluated carbonates **1d**, **1e**, and **1f** in the synthesis of α-nitro esters and the results are summarized in Table 2 (yields are unoptimized). All the reactions were monitored by TLC and quenched after complete consumption of starting materials. In the reaction with carbonate **1f**, the nitroalkane was consumed at a much faster rate than in the reaction with **1a**. Although the reaction was faster, the yield was lower possibly due to formation of side products.[3] We were unable to isolate

Table 2. Evaluating the Effect of Benzene Ring Substitution in the Synthesis of α-Nitro Esters



entry	carbonate	product	time[a]	% yield
1	**1a**	**4a**	5 h	77
2	**1d**	**4d**	5 h	74
3	**1e**	**4e**	3 h	70
4	**1f**	**4f**	1 h	48

[a]Reactions were quenched after complete consumption of starting materials.

and characterize these side-products. However, the faster reaction with carbonate **1f** indicated a possible role for cation−π interactions in the activation of carbonates. To quantify the increase in reaction rate with variation in benzyl group, we wanted to evaluate the rate constant for consumption of carbonate. However, the variable yields observed for formation of α-nitro esters precluded the possibility of using this reaction for a kinetic study. Therefore, we decided to study the activation of carbonates using a model reaction that would potentially go through a similar transition state. For this purpose, we chose the DABCO mediated hydrolysis of carbonates as our model reaction. The reaction of DABCO with a benzyl aryl carbonate generates an activated acyl group. In the case of α-nitro ester formation, the activated acyl group reacts with nitronate anion, while in our model reaction it is expected to react with water. Decompostion of the resulting benzyl hydrogen carbonate will yield the corresponding alcohol. DMSO was chosen as the solvent for this study as it was used as an additive in the synthesis of α-nitro esters.[2]

To examine the role of benzyl group, we synthesized various carbonates (Figure 1) and studied the kinetics of their hydrolysis under pseudo-first-order conditions in the presence of DABCO as a nucleophile. An 80:20 mixture of DMSO-d_6 and D_2O was used as solvent and the initial concentration of carbonate was 0.03 M. Reactions were performed in an NMR tube, which was immersed in an oil bath maintained at 40 °C. The percentage of carbonate remaining at various time points (C_t) was measured by comparing its integration with an internal standard. Rate constants were obtained by plotting $\ln(100/C_t)$ vs time (see Supporting Information) and the results are summarized in Table 3. Reactions were performed in

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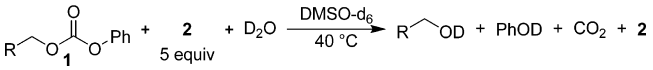
triplicate and average rate constants are reported (see Supporting Information for standard deviations).

Table 3. Rate Constants for Hydrolysis of Carbonates with DABCO as the Nucleophile

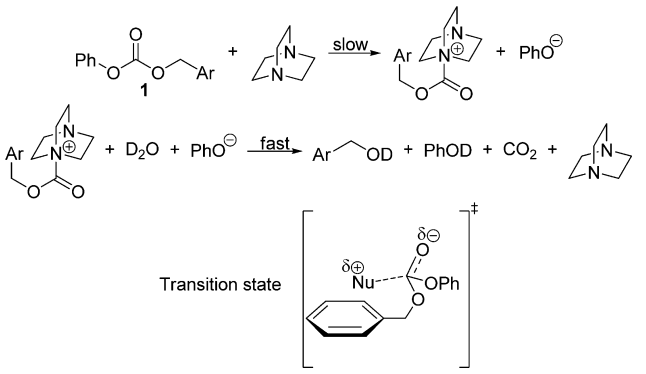


entry	carbonate	rate constant k (min^{-1})[a]	relative rate
1	**1c**	8.8×10^{-5}	1
2	**1a**	1.4×10^{-3}	16
3	**1d**	2.0×10^{-3}	23
4	**1e**	1.5×10^{-3}	17
5	**1f**	4.5×10^{-3}	51
6	**1g**	2.3×10^{-3}	26
7	**1h**	2.9×10^{-3}	33
8	**1i**	3.9×10^{-3}	44
9	**1j**	1.2×10^{-3}	14
10	**1k**	9.3×10^{-4}	11

[a]Reactions were performed in an NMR tube immersed in an oil bath maintained at 40 °C. For monitoring the reactions, the NMR tube was immersed in an ice bath for a few minutes followed by recording of spectra at 25 °C. All reactions were repeated thrice and the average k is reported. For standard deviations see Supporting Information.

We began our studies on hydrolysis of unsubstituted carbonate **1a**. The hydrolysis reached 92% conversion over 1900 min. A plot of $\ln(100/C_t)$ vs time gave an excellent linear fit and a rate constant of $k = 1.4 \times 10^{-3}$/min was obtained. Under similar conditions, the rate constant for hydrolysis of isobutyl phenyl carbonate **1c** was found to be 8.8×10^{-5}/min. The 16-fold acceleration in the presence of benzyl group can be rationalized by the hypothetical mechanism shown in Scheme 2. We hypothesize that the observed rate acceleration is due to

Scheme 2. Hypothetical Reaction Pathway for the Hydrolysis of Carbonate, with the Nucleophilic Attack of DABCO on the Carbonate as the Rate Determining Step[a]



[a]A plausible transition state that involves cation−π interaction is shown.

stabilization of the transition state by cation−π interactions between the acyl-ammonium cation and the benzene ring. The stabilization of the transition state is expected to be sensitive to the substitution pattern of the aromatic ring. Theoretical calculations have shown that in gas phase, toluene binds tetramethylammonium ion more strongly than benzene by 0.5 kcal/mol.[13a] On the other hand, thermochemical measurements have shown that the difference in binding energy between these systems is 0.1 kcal/mol.[13b] On the basis of these studies, we expected the transition state for hydrolysis of 4-methylbenzyl phenyl carbonate (**1g**) to be ∼0.1 to 0.5 kcal/mol more stable than the transition state for hydrolysis of **1a**. Corresponding to this, we expected the hydrolysis of **1g** to be faster than the hydrolysis of **1a**. Consistent with our hypothesis, the rate constant for hydrolysis of 4-methylbenzyl phenyl carbonate (**1g**) was higher ($k = 2.3 \times 10^{-3}$/min) than the rate constant for hydrolysis of carbonate **1a** ($k = 1.4 \times 10^{-3}$/min). This shows that the transition state for hydrolysis of carbonate **1g**, is 0.3 kcal/mol more stable than the transition state for hydrolysis of **1a**. With respect to hydrolysis of isobutyl phenyl carbonate **1c**, a 26-fold rate acceleration was observed. We then studied the hydrolysis of other carbonates shown in Figure 1. The 4-bromobenzyl phenyl carbonate (**1e**) hydrolyzed at the same rate as benzyl phenyl carbonate ($k = 1.5 \times 10^{-3}$/min), while the hydrolysis of naphthalenemethyl phenyl carbonates (**1d** and **1h**) were faster. Interestingly, the positional isomers showed different rates of hydrolysis, with carbonate **1h** hydrolyzing faster (relative rate ≈ 34) than carbonate **1d** (relative rate ≈ 23). The observed rate accelerations are consistent with greater stabilization of cation by extended π-systems.[14] Hydrolysis of carbonate **1f** was ∼51 times faster than the hydrolysis of carbonate **1c**. The hydrolysis of 3,4-dimethoxy benzyl phenyl carbonate **1i** is slightly slower than the hydrolysis of carbonate **1f** with a relative rate of ∼44. We attribute this to unfavorable steric interactions between the nucleophile and a meta substituent on the benzene ring. Consistent with this, the hydrolysis of 3-methoxy benzyl phenyl carbonate **1j** (relative rate ≈ 14) was slower than the hydrolysis of the 4-methoxy substituted carbonate **1f**. To probe the effect of an electron withdrawing group on the aromatic system, we studied the hydrolysis of the 4-CF_3 substituted carbonate **1k**. Electron-withdrawing groups on the benzene ring are expected to diminish cation−π interactions and indeed carbonate **1k** hydrolyzed at a slower rate than carbonate **1a**. For systematically analyzing the effect of substituents on the proposed transition state, we used Hammett plots.[15] In this study, we used carbonates **1a**, **1e**, **1f**, **1g**, and **1k** as the substituents on these carbonates have well-defined σ values. The logarithm of relative rate with respect to **1a** was plotted against various σ parameters. Correlation with σ_p and σ_p^- values[15] gave the best fits. (R^2 = 0.85 and 0.88 respectively. see Supporting Information). The corresponding ρ values were −1.84 and −1.66 respectively. The low values for ρ are possibly due to shielding of the cation from the aromatic system by solvent molecules.[16] Cation−π interactions are known to depend on the distance of the cationic group from the benzyl ring.[17] To test this, we synthesized the phenethyl carbonate **1l** and studied the hydrolysis under our standard conditions. The reaction was very slow and only ∼13% of the carbonate was consumed in 720 min. The reduction of hydrolysis rate in this case is attributable to the increased distance between the aromatic ring and the cationic center.

In order to test the generality of the cation−π induced rate acceleration, we decided to study the hydrolysis of carbonates using DMAP as the nucleophile. Previous work from the Mayr group has shown that DABCO is a better nucleophile than DMAP.[18] On the basis of our proposed transition state for the attack of nucleophile (Scheme 2), we expected the hydrolysis to be slower with the less nucleophilic DMAP. Indeed, to get appreciable rates of hydrolysis, the reactions had to be carried out at 60 °C. When we plotted $\ln(100/C_t)$ vs time (see

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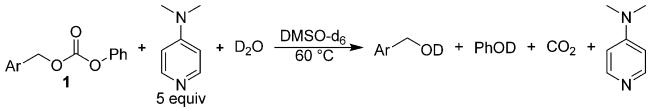
Supporting Information), we did not obtain straight lines. The reactions appeared to be faster at initial time points and settled down to a slower rate as the reaction progressed. Therefore, we were unable to compare rate constants. A qualitative idea about cation−π interaction could be obtained by comparing the time taken for the reaction to reach ∼90% completion. The results are summarized in Table 4. As expected, 4-methoxybenzyl

Table 4. Hydrolysis of Carbonates with DMAP as the Nucleophile[a]



		time (approximately 90% completion)[b]	
entry	carbonate	run 1	run 2
1	**1a**	39 h (90%)	41 h (90%)
2	**1d**	20 h (89%)	20 h (89%)
3	**1f**	6.5 h (92%)	6.2 h (89%)
4	**1h**	19 h (90%)	21 h (91%)
5	**1i**	5 h (92%)	5 h (90%)

[a]Time taken for the reactions to reach ∼90% completion are given. [b]Reactions were performed at 60 °C and monitored as mentioned in Table 3.

phenyl carbonate (**1f**) hydrolyzed ∼6 times faster than the unsubstituted carbonate **1a**. In contrast to the reaction with DABCO, the dimethoxy substituted carbonate (**1i**) also hydrolyzed at the same rate as the 4-methoxy substituted carbonate (**1f**). Similarly, a significant acceleration is seen in the hydrolysis of the naphthalenemethyl phenyl carbonates (**1h**, **1d**). Here, the positional isomers are hydrolyzed at a similar rate. On the basis of the above results, it is clear that the cation−π interactions play an important role in activating benzyl phenyl carbonates. Activated acyl groups have been used in many reactions including kinetic resolution of alcohols and enantioselective *O*- to *C*-carboxyl transfer.[5,6] In kinetic resolutions of secondary alcohols, an anhydride is typically used as a source of activated acyl group.[12c,d] Benzyl carbonates are more stable than acid anhydrides and are also easily purified. Therefore, these reagents could potentially replace acid anhydrides as acyl donors. Cation−π interactions appear to be important in stabilizing the transition state for nucleophilic attack of these carbonates. Varying the substituents on the aromatic ring of the benzyl group can tune this interaction and facilitate rapid activation of these stable carbonates.

CONCLUSIONS

We have studied the hydrolysis of benzyl aryl carbonates mediated by nucleophiles. Rate constants for reactions mediated by DABCO were obtained under pseudo-first-order conditions. Comparison of the rate constant for hydrolysis of isobutyl phenyl carbonate with various substituted benzyl carbonates showed that cation−π interactions play an important role in hydrolysis. Importantly, 4-methoxybenzyl phenyl carbonate hydrolyzed at a faster rate than naphthalenemethyl phenyl carbonate. This indicates that a 4-methoxybenzyl group might stabilize an ammonium cation better than a naphthalenemethyl group. When hydrolyses were performed with DMAP, we were unable to get good straight line fits for our data. Therefore, rates of hydrolysis were compared in a qualitative manner and trends similar to DABCO mediated hydrolysis were observed. Nucleophilic activation leads to generation of a strong base along with an activated acyl group. Together, this can be a useful tool for exploring new reactivity patterns. Typically, activated acyl groups are generated from the much more reactive acid anhydrides, whereas in our approach this can be generated from stable and easy-to-purify carbonates. Further work in our group will focus on developing novel transformations using this system.

EXPERIMENTAL SECTION

All glassware was dried overnight in an oven at 120 °C prior to use. Reactions were carried out under argon atmosphere using standard Schlenk techniques and were monitored by thin layer chromatography (TLC) using silica gel TLC plates. Flash column chromatography was performed using silica gel of mesh size 230−400. Grease-free solvents for flash column chromatography were obtained by distillation. Unless otherwise noted, all chemicals obtained from commercial sources were used without further purification. Infrared spectra were recorded using an FT-IR Spectrometer. ^{1}H and ^{13}C NMRs were recorded on a 400 MHz Fourier Transform NMR spectrometer. Chemical shifts are reported in parts per million (ppm) with respect to the residual solvent peak. For ^{1}H NMRs recorded in $CDCl_3$, the residual solvent peak at 7.27 ppm was used for calibration. For {^{1}H} ^{13}C NMRs recorded in $CDCl_3$, the residual solvent peak at 77.16 ppm was used for calibration. For ^{1}H NMRs recorded in DMSO-d_6, the residual solvent peak at 2.50 ppm was used for calibration. For {^{1}H} ^{13}C NMRs recorded in DMSO-d_6, the residual solvent peak at 39.5 ppm was used for calibration. ^{13}C NMRs were recorded at 100 MHz using proton decoupling. HRMS were recorded using Q-TOF mass analyzer. Melting points were measured using melting point apparatus.

General Procedure for the Synthesis of Carbonates. Two general procedures were adapted from literature.[2]

Method A. A round bottomed flask was charged with phenol (1 equiv), dichloromethane (DCM), and pyridine (1.26 equiv). The flask was immersed in an ice bath and benzyl chloroformate (1.3 equiv) was added dropwise. The reaction mixture was allowed to warm up to room temperature and stirred overnight. The reaction mixture was transferred to a separatory funnel and diluted with DCM. The organic layer was washed successively with deionized water, 5% NaOH, 1 M HCl, and brine. The organic layer was dried over Na_2SO_4 and concentrated. The material obtained was purified by flash column chromatography.

Method B. A round bottomed flask was charged with the required benzyl alcohol (1 equiv), DCM, and pyridine (1.26 equiv). The flask was immersed in an ice bath and phenyl chloroformate (1.3 equiv) was added dropwise. The reaction mixture was allowed to warm up to room temperature and stirred overnight. The reaction mixture was transferred to a separatory funnel and diluted with DCM. The organic layer was washed successively with deionized water, 5% NaOH, 1 M HCl and brine. The organic layer was dried over Na_2SO_4 and concentrated. The material obtained was purified by flash column chromatography.

Benzyl phenyl carbonate (1a). Method A was employed with the following quantities: phenol (4.68 g, 49.7 mmol), benzyl chloroformate (2.93 M solution in toluene, 22 mL (64.7 mmol), pyridine (5 mL, 62.5 mmol), and DCM (50 mL).

Column Chromatography. Approximately 150 mL of silica was packed into a column using 20% DCM in hexanes as the solvent. The material obtained from workup was loaded on the column after dissolution in a minimum amount of this solvent. Approximately 500 mL of 20% DCM in hexanes was eluted followed by elution with 1200 mL of 25% DCM in hexanes. The eluted solvent was collected in 25 mL fractions. Fractions 21−63 contained product. These fractions were concentrated and dried under high vacuum to give 6.46 g of product (yield: 57%). The ^{1}H NMR of the product was in agreement with the literature.[19]

***tert*-Butyl phenyl carbonate (1b).** Method B was employed with the following quantities: *tert*-butyl alcohol (3.4 mL, 35.55 mmol),

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phenyl chloroformate (5.8 mL, 46.2 mmol), pyridine (3.7 mL, 45.9 mmol), and DCM (35 mL).

Column Chromatography. Approximately 130 mL of silica was packed into a column using 2% ethyl acetate (EtOAc) in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 800 mL of 2% EtOAc in hexanes was eluted. The eluted solvent was collected in 25 mL fractions. Fractions 6−27 contained product. These fractions were concentrated and dried under high vacuum to give 4.1 g of product (yield: 88%). The ^{1}H NMR data of the product was in agreement with the literature.[20]

2-Methylpropyl phenyl carbonate (1c). Method A was modified by replacing benzyl chloroformate with isobutylchloroformate and the following quantities were used: isobutyl chloroformate (3 mL, 23.1 mmol), phenol (3.24 g, 34.4 mmol), pyridine (3.5 mL, 43.4 mmol), and DCM (35 mL).

Column Chromatography. Approximately 100 mL of silica was packed into a column using 25% DCM in hexanes as the solvent. The material obtained from work up was loaded on the column after dissolution in a minimum amount of this solvent. Approximately 1000 mL of 25% DCM in hexanes was eluted. The eluted solvent was collected in 25 mL fractions. Fractions 4−29 contained product. These fractions were concentrated and dried under high vacuum to give 3.1 g of product (yield: 69%).

Characterization. Colorless liquid; R_f 0.36 in 10% EtOAc in hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.37 (m, 2H), 7.27−7.17 (m, 3H), 4.05 (d, J = 6.7 Hz, 2H), 2.07 (m, 1H), 1.06 (d, J = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 151.3, 129.6, 126.1, 121.2, 74.9, 28.0, 19.0; IR (film):1758, 1237, 1204, 768 cm^{-1}; HRMS (ESI): m/z (M + Na)$^+$ Calcd for $C_{11}H_{14}NaO_3^+$ 217.0841, found 217.0832.

Naphthalen-2-ylmethyl phenyl carbonate (1d). Method B was employed with the following quantities: naphthalene-2-ylmethanol (4 g, 25.32 mmol), phenyl chloroformate (4.8 mL, 38.26 mmol), pyridine (2.7 mL, 33.5 mmol), and DCM (25 mL).

Column Chromatography. Approximately 110 mL of silica was packed into a column using 1.1% EtOAc in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 1600 mL of 1.1% EtOAc in hexanes was eluted. The eluted solvent was collected in 25 mL fractions. Fractions 34−62 contained product. These fractions were concentrated and dried under high vacuum to give 2.03 g of product (yield: 29%).

Characterization. Pale brown crystalline solid; mp = 45−46 °C; R_f 0.2 in 2.5% EtOAc in hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.5 Hz, 1H), 7.93−7.90 (m, 2H), 7.65−7.54 (m, 3H), 7.49 (dd, J = 7.1, 8.2 Hz, 1H), 7.41−7.36 (m, 2H), 7.25−7.17 (m, 3H), 5.76 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 151.3, 133.9, 131.0, 130.5, 130.0, 129.6, 128.9, 128.2, 127.0, 126.22, 126.17, 125.4, 123.6, 121.2, 68.7; IR (film):1763, 1244, 1212, 976, 772 cm^{-1}; HRMS (ESI) m/z (M + Na)$^+$ Calcd for $C_{18}H_{14}NaO_3^+$ 301.0841, found 301.0838.

4-Bromobenzyl phenyl carbonate (1e). Method B was employed with the following quantities: 4-bromobenzyl alcohol (3.41 g, 18.22 mmol), phenyl chloroformate (3.5 mL, 27.8 mmol), pyridine (2 mL, 24.8 mmol), and DCM (20 mL).

Column Chromatography. Approximately 110 mL of silica was packed into a column using 25% DCM in hexanes as the solvent. The material obtained from workup was loaded on the column after dissolution in a minimum amount of this solvent. Approximately 1300 mL of 25% DCM in hexanes was eluted and collected in 25 mL fractions. Fractions 8−53 contained product. The fractions were concentrated. However, the isolated compound contained diphenyl carbonate. This mixture was purified by column chromatography, using 110 mL silica. Approximately 1200 mL of 0.77% EtOAc in hexanes was eluted followed by 300 mL of DCM and 25 mL fractions were collected. Fractions 45−61 contained pure compound. These fractions were concentrated and dried under high vacuum to give 2.6 g of product (yield: 46%).

Characterization. Pale yellow liquid; R_f 0.13 in 30% DCM in hexanes; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.63−7.61 (m, 2H), 7.46−7.41 (m, 4H), 7.31−7.23 (m, 3H), 5.25 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.9, 150.7, 134.5, 131.5, 130.5, 129.6, 126.2, 121.8, 121.2, 68.9; IR (film): 1759, 1492, 1201, 1012, 772, 496 cm^{-1}; HRMS (ESI) m/z (M + Na)$^+$ Calcd for $C_{14}H_{11}BrNaO_3^+$ 328.9789, found 328.9787.

4-Methoxybenzyl phenyl carbonate (1f). Method B was employed with the following quantities: 4-methoxybenzyl alcohol (4 g, 28.95 mmol), phenyl chloroformate (4.7 mL, 37.46 mmol), pyridine (3 mL, 37.2 mmol), and DCM (30 mL).

Column Chromatography. Approximately 110 mL of silica was packed into a column using 0.7% EtOAc in hexanes as the solvent. The material obtained from workup was loaded on the column after dissolution in a minimum amount of this solvent. Approximately 1100 mL of 0.7% EtOAc in hexanes was eluted followed by elution with 400 mL of 30% DCM in hexanes. The eluted solvent was collected in 25 mL fractions. Fractions 33−53 contained pure product. These fractions were concentrated and dried under high vacuum to give 5.07 g of product (yield: 68%). The ^{1}H NMR data of the product was in agreement with the literature.[19]

4-Methylbenzyl phenyl carbonate (1g). Method B was employed with the following quantities: 4-methylbenzyl alcohol (2 g, 16.37 mmol), phenyl chloroformate (2.7 mL, 21.5 mmol), pyridine (1.6 mL, 19.9 mmol), and DCM (16 mL).

Column Chromatography. Approximately 110 mL of silica was packed into a column using 1% EtOAc in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 1100 mL of 1% EtOAc in hexanes was eluted followed by elution with 500 mL of 15% EtOAc in hexanes. The eluted solvent was collected in 25 mL fractions. Fractions 3−20 contained product. These fractions were concentrated and dried under high vacuum to give 2.88 g of product (yield: 73%). The ^{1}H NMR, data of the product was in agreement with the literature.[21]

Naphthalen-1-ylmethyl phenyl carbonate (1h). Method B was employed with the following quantities: naphthalene-1-ylmethanol (1.73 g, 10.9 mmol), phenyl chloroformate (1.7 mL, 13.5 mmol), pyridine (1 mL, 12.4 mmol), and DCM (10 mL).

Column Chromatography. Approximately 90 mL of silica was packed into a column using 1% EtOAc in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 1400 mL of 1% EtOAc in hexanes was eluted. The eluted solvent was collected in 25 mL fractions. Fractions 26−44 contained product. These fractions were concentrated and dried under high vacuum to give 1.79 g of product (yield: 59%).

Characterization. Crystalline white solid; mp = 43−44 °C; R_f 0.4 in 5% EtOAc in hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.2 Hz, 1H), 7.93−7.90 (m, 2H), 7.65−7.54 (m, 3H), 7.49 (dd, J = 7.6, 8.2 Hz, 1H), 7.41−7.37 (m, 2H), 7.25−7.18 (m, 3H), 5.76 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 151.2, 133.8, 131.6, 130.3, 129.8, 129.5, 128.8, 128.1, 126.8, 126.1, 126.0, 125.3, 123.5, 121.0, 68.6; IR (film): 1757, 1246, 1206, 1068, 974, 771, 686 cm^{-1}; HRMS (ESI) m/z (M + Na)$^+$ Calcd for $C_{18}H_{14}NaO_3^+$ 301.0841, found 301.0835.

3,4-Dimethoxybenzyl phenyl carbonate (1i). Method B was employed with the following quantities: 3,4-dimethoxybenzyl alcohol (3.068 g, 18.24 mmol), phenyl chloroformate (3.5 mL, 27.9 mmol), pyridine (1.9 mL, 23.6 mmol), and DCM (18 mL).

Column Chromatography. Approximately 100 mL of silica was packed into a column using 8% EtOAc in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 900 mL of 8% EtOAc in hexanes was eluted followed by elution with 300 mL of 15% EtOAc in hexanes and 200 mL of 20% EtOAc in hexanes. The eluted solvent was collected in 25 mL fractions. Fractions 25−49 contained product. These fractions were concentrated and dried under high vacuum to give 4.18 g of product (yield: 80%).

Characterization. Crystalline white solid; mp = 47−48 °C; R_f 0.16 in 20% EtOAc in hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.36 (m, 2H), 7.27−7.17 (m, 3H), 7.04−6.98 (m, 2H), 6.89−6.87 (m, 1H), 5.22 (s, 2H), 3.92 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 151.3, 149.7, 149.2, 129.6, 127.4, 126.2, 121.9, 121.2, 112.1,

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111.2, 70.7, 56.1; IR (film): 1739, 1247, 1023, 748, 705 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.88; H, 5.62.

3-Methoxybenzyl phenyl carbonate (1j). Method B was employed with the following quantities: 3-methoxybenzyl alcohol (960 μL, 7.72 mmol), phenyl chloroformate (1.2 mL, 9.6 mmol), pyridine (800 μL, 9.93 mmol), and DCM (8 mL).

Column Chromatography. Approximately 80 mL of silica was packed into a column using 3% EtOAc in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 600 mL of 3% EtOAc in hexanes was eluted followed by elution with 400 mL of 8% EtOAc in hexanes. The eluted solvent was collected in 25 mL fractions. Fractions 14−25 contained product. These fractions were concentrated and dried under high vacuum to give 1.39 g of product (yield: 70%).

Characterization. White viscous liquid; R_f 0.16 in 5% EtOAc in hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.37 (m, 2H), 7.34−7.30 (m, 1H), 7.25−7.18 (m, 3H), 7.04−6.91 (m, 3H), 5.26 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 153.8, 151.3, 136.4, 129.9, 129.6, 126.2, 121.2, 120.8, 114.6, 113.9, 70.3, 55.4; IR (film): 1755, 1590, 1205, 1039, 685, 504 cm^{-1}; HRMS (ESI) m/z $(M + Na)^+$ Calcd for $C_{15}H_{14}NaO_4^+$ 281.0790; Found: 281.0790.

4-Trifluoromethylbenzyl phenyl carbonate (1k). Method B was employed with the following quantities: 4-trifluoromethylalcohol (650 mg, 3.69 mmol), phenyl chloroformate (700 μL, 5.1 mmol), pyridine (420 μL, 5.21 mmol), and DCM (6 mL)

Column Chromatography. Approximately 96 mL of silica was packed into a column using 2% EtOAc in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 1400 mL of 2% EtOAc in hexanes was eluted. The eluted solvent was collected in 25 mL fractions. Fractions 39−56 contained product. These fractions were concentrated and dried under high vacuum to give 611 mg of product (yield: 56%).

Characterization. Crystalline white solid; mp = 62−64 °C; R_f 0.16 in 2% EtOAc in hexanes; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.79 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 8.1 Hz, 2H), 7.47−7.42 (m, 2H), 7.32−7.25 (m, 3H), 5.38 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 154.1, 152.0, 141.1, 130.9, 129.8, 127.5, 126.7 (q, J = 3.6 Hz), 124.0, 122.4, 70.0; IR (film): 1750, 1275, 1105, 1066, 715 cm^{-1}; HRMS (ESI) m/z $(M + Na)^+$ Calcd for $C_{15}H_{11}F_3O_3Na^+$ 319.0558; Found: 319.0557.

Phenyl-2-phenylethyl carbonate (1l). Method B was employed with the following quantities: 2-phenylethanol (4 mL, 33.3 mmol), phenyl chloroformate (5.4 mL, 43.04 mmol), pyridine (3.4 mL, 42.2 mmol), and DCM (30 mL).

Column Chromatography. Approximately 110 mL of silica was packed into a column using 0.7% EtOAc in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 1100 mL of 0.7% EtOAc in hexanes was eluted followed by elution of 1100 mL of 30% DCM in hexanes. The eluted solvent was collected in 25 mL fractions. Fractions 45−84 contained product. These fractions were concentrated and dried under high vacuum to give 6.63 g of product (yield: 82%).

Characterization. Amorphous white solid; mp = 79−80 °C ;R_f 0.16 in 2.5% EtOAc in hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.33 (m, 4H), 7.29−7.28 (m, 2H), 7.26−7.23 (m, 2H), 7.17−7.14 (m, 2H), 4.47 (t, J = 7.1 Hz, 2H), 3.07(t, J = 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 151.1, 137.0, 129.5, 129.0, 128.6, 126.8, 126.0, 121.1, 69.0, 35.1 ; IR (film):1751, 1486, 1262, 969, 757, 704, 501 cm^{-1}; HRMS (ESI) m/z $(M + Na)^+$ Calcd for $C_{15}H_{14}NaO_3^+$ 265.0840, found 265.0835.

General Procedure for the Synthesis of Nitroesters. A thick-walled glass tube with a Teflon screw cap was charged with phenylnitroethane (1equiv) and aryl phenyl carbonate (3 equiv). The tube was flushed with argon and dimethyl sulfoxide (3 equiv) was added followed by 1,4-diazabicyclo [2.2.2] octane (DABCO) (2 equiv). The tube was capped and immersed in an oil bath at 60 °C. The reaction mixture was stirred at this temperature and the progress of the reaction was monitored by TLC.

Workup Procedure. After completion of reaction by TLC, the reaction mixture was cooled to 0 °C and quenched with 1 M $KHSO_4$. This was further stirred at room temperature until a suspension was formed. The suspension was transferred to a separatory funnel containing 15 mL of 1 M $KHSO_4$. The aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined ether layers were dried over Na_2SO_4, concentrated, and purified by flash column chromatography.

Benzyl 2-nitro-3-phenylpropanoate (4a). The general procedure was employed with the following quantities: 2-phenylnitro ethane (100 mg, 0.66 mmol), **1a** (455 mg, 2.0 mmol), DABCO (150 mg, 1.33 mmol), and DMSO (140 μL, 2.0 mmol). Time: 5 h.

Column Chromatography. Approximately 50 mL of silica was packed into a column using 25% DCM in hexanes as the solvent. The material obtained from workup was loaded on the column after dissolution in a minimum amount of this solvent. Approximately 800 mL of 25% DCM in hexanes was eluted followed by elution with 400 mL of 40% DCM in hexanes. The eluted solvent was collected in 12 mL fractions. Fractions 58−67 contained product, diphenyl carbonate and phenyl benzyl carbonate. Fractions 68−71 contained pure product. Fractions 58−67 were concentrated and purified by column chromatography. Approximately 40 mL of silica was packed into a column using 3% EtOAc in hexanes as the solvent. The mixed fractions from the first column was adsorbed on silica and loaded on the column. Approximately 450 mL of 3% EtOAc in hexanes was eluted followed by elution with 100 mL of 50% DCM in hexanes. The eluted solvent was collected in 12 mL fractions. Fractions 36−38 contained product. The fractions containing pure product from column I and column II were concentrated and dried under high vacuum to give 149 mg of product (yield: 78%). The ^{1}H NMR, data of the product was in agreement with the literature.[2]

Naphthalen-2-ylmethyl 2-nitro-3-phenylpropanoate (4d). The general procedure was employed with the following quantities: 2-phenylnitro ethane (75 mg, 0.5 mmol), **1d** (415 mg, 1.5 mmol), DABCO (112 mg, 1 mmol), and DMSO (110 μL, 1.5 mmol). Time: 5 h.

Column Chromatography. Approximately 45 mL of silica was packed into a column using 3% EtOAc in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 700 mL of 3% EtOAc in hexanes was eluted. The eluted solvent was collected in 25 mL fractions. Fractions 15−22 contained product. These fractions were concentrated and dried under high vacuum to give 135 mg of product. The obtained product contained 7.5 mol % of bis(naphthalene-2-ylmehtyl) carbonate as impurity. Yield: 74% (based on ^{1}H NMR).

Characterization. Brown viscous liquid; R_f 0.23 in 5% EtOAc in hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.86 (m, 3H), 7.59−7.43 (m, 5H), 7.26−7.24 (m, 3H), 7.15−7.12 (m, 2H), 5.70 (s, 2H), 5.37 (dd, J = 6.2, 9.1 Hz, 1H), 3.56 (dd, J = 9.1, 14.4 Hz, 1H), 3.46 (dd, J = 6.2, 14.4 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 133.93, 133.90, 131.7, 130.2, 129.8, 129.1, 129.0, 128.96, 128.3, 127.9, 127.1, 126.3, 125.3, 123.3, 89.1, 67.2, 36.4; IR (film): 1747, 1562, 1202, 1170, 859, 777, 701 cm^{-1}; HRMS (ESI) m/z $(M-H)^-$ Calcd for $C_{20}H_{16}NO_4^-$, 334.1084, found, 334.1081.

4-Bromobenzyl 2-nitro-3-phenylpropanoate (4e). The general procedure was employed with the following quantities: 2-phenylnitro ethane (75 mg, 0.5 mmol), **1e** (456 mg, 1.5 mmol), DABCO (112 mg, 1 mmol), and DMSO (110 μL, 1.5 mmol). Time: 3 h.

Column Chromatography. Approximately 45 mL of silica was packed into a column using 25% toluene in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 1300 mL of 25% toluene in hexanes was eluted. The eluted solvent was collected in 25 mL fractions. Fractions 35−49 contained product. These fractions were concentrated and dried under high vacuum to give 127 mg of product (yield: 70%).

Characterization. Brown viscous liquid; R_f 0.16 in 50% DCM in hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.48 (m, 2H), 7.33−7.28 (m, 3H), 7.19−7.13 (m, 4H), 5.37 (dd, J = 6.3, 9.1 Hz, 1H), 5.17 (s, 2H), 3.57 (dd, J = 9.1, 14.5 Hz, 1H), 3.48 (dd, J = 6.3, 14.5 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 133.9, 133.3, 132.1, 130.2, 129.2, 129.0, 128.0, 123.2, 89.1, 67.9, 36.4; IR (film): 1747,

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1562, 1489, 1198, 1174, 802, 697 cm^{-1}; HRMS (ESI) m/z $(M-H)^-$ Calcd for $C_{16}H_{13}BrNO_4^-$, 362.0033, found 362.0028.

4-Methoxybenzyl 2-nitro-3-phenylpropanoate (4f). The general procedure was employed with the following quantities: 2-phenylnitro ethane (75 mg, 0.5 mmol), **1f** (384 mg, 1.5 mmol), DABCO (112 mg, 1 mmol), and DMSO (110 μL, 1.5 mmol). Time: 1 h.

Column Chromatography. Approximately 45 mL of silica was packed into a column using 60% toluene in hexanes as the solvent. The material obtained from workup was adsorbed on silica and loaded on the column. Approximately 400 mL of 60% toluene in hexanes was eluted followed by the elution of 400 mL of 70% toluene in hexanes. The eluted solvent was collected in 25 mL fractions. Fractions 16−22 contained product. These fractions were concentrated and dried under high vacuum to give 82 mg of product. The obtained product contains 7.5 mol % of bis(4-methoxybenzyl) carbonate as impurity. Yield: 48% (based on ^1H NMR).

Characterization. Brown viscous liquid; R_f 0.16 in 30% DCM in hexanes; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31−7.27 (m, 3H), 7.25−7.15 (m, 4H), 6.89−6.87 (m, 2H), 5.34 (dd, J = 6.0, 9.2 Hz, 1H), 5.17 (s, 2H), 3.81 (s, 3H), 3.54 (dd, J = 9.4, 14.5 Hz, 1H), 3.45 (dd, J = 6.0, 14.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 160.3, 134.1, 130.6, 129.1, 129.0, 127.9, 126.4, 114.3, 89.3, 68.7, 55.5, 36.4; IR (film): 1747, 1614, 1558, 1513, 1250, 1174, 1028, 826, 701 cm^{-1}; HRMS (ESI) m/z $(M-H)^-$ Calcd for $C_{17}H_{16}NO_5^-$, 314.1034, found 314.1024.

Hydrolysis of Carbonates with DABCO. A 1 mL volumetric flask was charged with 1 mg of naphthalene (as an internal standard) and 0.03 mmol (1 equiv) of carbonate. To this 600 μL of DMSO-d_6 was added. Carbonate and naphthalene were dissolved in the solvent followed by the addition of 200 μL of D_2O. To this, 5.1 equiv (±7%) of DABCO was added and the solution was made up to the mark using DMSO. The solution was immediately transferred to a clean NMR tube and ^1H NMR spectra were recorded at regular intervals.

Note: For hydrolysis of carbonate **1c**, the ASCII files of NMR were exported to origin and integration of peaks was performed in origin.

Hydrolysis of Carbonates with DMAP. A 1 mL volumetric flask was charged with 1 mg of naphthalene (as an internal standard)[22] and 0.03 mmol (1 equiv) of carbonate. To this 600 μL of DMSO-d_6 was added. Carbonate and naphthalene were dissolved in the solvent followed by the addition of 200 μL of D_2O. To this, 5 equiv (±2%) of DMAP was added and the solution was made up to the mark using DMSO. The solution was immediately transferred to a clean NMR tube and ^1H NMR spectra were recorded at regular intervals.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00441.

Kinetic plots, Hammett plots and NMR spectra. (PDF)

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Notes

The authors declare no competing financial interest.

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