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Mild and Efficient Capture and Functionalisation of CO₂ using Silver(I) Oxide and Application to ¹³C-labelled Dialkyl Carbonates

Gemma A. Tunbridge,^a Riccardo Baruchello^{a,b} and Lorenzo Caggiano^{*a}

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A high yielding three-component reaction between β-iodo ethylamine derivatives, MeOH and gaseous CO₂ at ambient temperatures and pressures is reported using silver(I) oxide. Unfunctionalised alkyl iodides were also found to be effective in this transformation and their optimisation is also described. To highlight the ease and control at which gaseous CO₂ can be captured and functionalised under mild conditions, the reaction was performed using ¹³C-enriched CO₂ to afford specifically ¹³C-carbonyl-labelled dialkyl carbonates with exquisite control of the isotopic purity in good yields and without the need for specialised equipment.

Introduction

The preparation of industrial chemicals from CO₂ is very attractive since CO₂ is a renewable source of carbon and has been implicated in climate change.^{1, 2} CO₂ is readily available, non-toxic and inexpensive, therefore any technology that can functionalise CO₂ under mild conditions will be of great industrial and academic interest.

Acyclic and cyclic carbonates are important intermediates for the synthesis of fine chemicals,³ plastics and polymers,⁴ fuels,^{5, 6} pharmaceuticals,⁷ solvents for asymmetric catalysis^{8, 9} and medical applications.^{10, 11} Various methods for the preparation of organic carbonates are known^{3, 12} and numerous reports use CO₂ as a starting material.^{2, 13-23} A common approach is by the nucleophilic capture of CO₂. The deprotonation of an alcohol with various bases has been reported to generate a nucleophile capable of capturing CO₂ which upon alkylation affords the corresponding carbonate or carbamate (A=O or NR² respectively, Scheme 1).²⁴⁻³¹

The reaction typically requires elevated temperatures, high pressures of CO₂, polar solvents and/or strong bases. Cs₂CO₃ has been used as both the base and a source of CO₂ through thermal decomposition.²⁴ With the addition of CO₂ gas however, the reaction can be performed at ambient temperature and the

Scheme 1 General scheme for nucleophilic capture of CO₂

Cs₂CO₃ acts solely as a base.²⁵ This reaction was then further developed and performed on solid-support and affords carbamate compounds from the corresponding amine.²⁶⁻²⁸ Allenamides have also been reported to capture CO₂ and cyclise in the presence K₂CO₃ or Cs₂CO₃ as a base to afford the corresponding cyclic carbamates.³⁰

Carbonate and carbamate groups have found various applications, including medicinal chemistry where they have been used as a temporary linker in pro-drugs derived from capuramycin,³² Taxol®³³⁻³⁵ and disease activated drugs (DAD).³⁶ Previous reports however suggest that some carbonate pro-drugs decompose during synthesis, possibly due to the basic reaction conditions employed. Silver complexes have been recently reported as CO₂ fixation catalysts, generating cyclic carbonates from epoxides.³⁷ Silver(I) salts have also been used in combination with DBU as the base to generate cyclic carbonates from propargyl alcohols and CO₂.³⁸ The reaction proceeds through the initial capture of CO₂ by the deprotonated alcohol and activation of the alkyne by the silver results in cyclisation of the intermediate to afford the cyclic carbonate. Subsequent reports have shown that under similar conditions tertiary and secondary propargyl alcohols afford the corresponding α,β-unsaturated carbonyl compound in high yields via a Meyer-Schuster type reaction.³⁹ The reaction has recently been extended to propargyl amines which generate the corresponding oxazolidinones under similar conditions.⁴⁰ Silver(I) salts in the presence of Cs₂CO₃ has also been reported to carbonylate terminal alkynes at ambient CO₂ pressures in very high yields.⁴¹

^a Medicinal Chemistry, Department of Pharmacy and Pharmacology,

University of Bath, Claverton Down, Bath, BA2 7AY. E-mail: l.caggiano@bath.ac.uk; Fax: +44 1225 386114; Tel: +44 1225 385709

^b Dipartimento di Scienze Farmaceutiche, Via Fossato di Mortara 17-19, Università di Ferrara, 44100 Ferrara, Italy.

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Table 1 Capture and functionalisation of CO₂ using *N,N*-dibenzyl β-iodo ethylamine **1a/b**, MeOH and Ag₂O^a

Entry	R-I	Ag(I)X (1.1 equiv.)	atmosphere	MeOH (equiv.)	Time	Yield (%)					
						1	2	3/6	4	5	7/8
1	1a	Ag ₂ O	CO ₂	25	35 min.	-	95, 2a	-	-	-	-
2	1b	Ag ₂ O	CO ₂	25	16 h	-	99, 2b	-	-	-	-
3	1a	Ag ₂ O	N ₂	25	35 min.	-	-	91, 3a	-	-	-
4	1b	Ag ₂ O	N ₂	25	16 h	-	-	98, 3b	-	-	-
5 ^b	1b	Ag ₂ O	CO ₂	-	16 h	-	-	-	94, 4b	-	-
6 ^{b,c}	1a	Ag ₂ O	air	-	16 h	35, 1a	-	15, 6a	7, 4a	43, 5a	-
7	1a	Ag ₂ O	CO ₂	5	3 h	-	95, 2a	-	-	-	-
8 ^c	1a	Ag ₂ CO ₃	air	5	3 h	-	36, 2a	17, 3a	26, 4a	21, 5a	-
9 ^c	1a	Ag ₂ CO ₃	CO ₂	5	3 h	-	73, 2a	-	10, 4a	17, 5a	-
10 ^c	1a	Ag ₂ CO ₃ ^d	air	5	2.5 h	-	17, 2a	-	69, 4a	14, 5a	-
11	1a	AgCl	CO ₂	25	16 h	-	-	-	-	-	87, 7a
12 ^e	1a	AgCl	CO ₂	25	16 h	-	-	-	-	-	99, 7a
13 ^c	1a	AgF	CO ₂	25	16 h	-	-	55, 3a	-	-	45, 8a

^a All reactions were performed at 20 °C in CHCl₃ under a balloon filled with CO₂ generated from melting dry ice, except where indicated. Yields are of isolated compounds, except where indicated. ^b CH₂Cl₂ was used as solvent. ^c The ratios were obtained from ¹H NMR of the crude reaction mixture after it had been filtered through Celite® and the solvent removed under reduced pressure. ^d 5 equivalents of Ag₂CO₃ were used. ^e MeCN was used as the solvent.

An unusual carbonate saccharide was obtained from the reaction of a chlorinated sugar derivative and geraniol in pyridine in the presence of Ag₂CO₃ for 8 days in 13% yield.⁴² Further studies revealed primary and secondary alcohols react with alkyl halides in the presence of 5 equivalents of Ag₂CO₃ in DMF to afford the corresponding unsymmetrical dialkylcarbonates.^{43, 44} The choice of solvent was found to be crucial as DMF gave the carbonate in 60% and in CH₂Cl₂ only the corresponding ether **15** was isolated in 21% yield (Scheme 2).⁴³ Reducing the amount of MeI and Ag₂CO₃ resulted in poor yields of the carbonate.

Scheme 2 Carbonate formation with Ag₂CO₃ in DMF and ether in CH₂Cl₂.⁴³

Results and Discussion

During our investigations in the synthesis of biologically active compounds, we discovered that *N,N*-dibenzyl β-iodo ethylamine **1a** in the presence of CO₂, Ag₂O and an excess of MeOH gave the unsymmetrical carbonate **2a** in 95% yield after only 35 minutes (entry 1, Table 1). The anisyl derivative **1b** was left for 16 h under the same conditions and gave the corresponding unsymmetrical carbonate **2b** quantitatively (entry 2). The CO₂ was generated by melting dry ice and capturing the released gas with a balloon which was then used directly in the reaction; no specialist equipment was used. Performing these reactions under a nitrogen atmosphere gave the corresponding

methyl ether **3a** or **3b** exclusively in 91% and 99% yield respectively (entries 3 and 4). Formation of the methyl ether **3** is the competing reaction and is simply the product of nucleophilic substitution of the alkyl iodide **1** with MeOH, mediated by the silver, as previously reported in Scheme 2.⁴³ These results demonstrate the facile and efficient functionalisation of gaseous CO₂ under mild reaction conditions.

In the absence of MeOH only the symmetrical carbonate **4b** was obtained in 94% yield (entry 5, Table 1). In the absence of both CO₂ and MeOH the reaction gave a mixture of compounds determined by ¹H NMR, which included unreacted starting material **1a** (35%), the corresponding alcohol **5a** (43%), the symmetrical carbonate **4a** (7%) and the symmetrical ether **6a** (15%, entry 6). The alcohol **5a** could be the product of reaction between the alkyl iodide **1a** (R-I) and Ag₂O generating the corresponding silver alkoxide (R-OAg) and AgI. Subsequent work up of the alkoxide with Celite® then affords the observed alcohol **5a**. Likewise, the symmetrical ether **6a** is presumably the product obtained from the reaction between the alkyl iodide **1a** and the alcohol **5a** (or silver alkoxide), in the absence of MeOH. Given that the atmosphere is composed of mostly N₂ (78%) and O₂ (21%) and only minute quantities of CO₂ (0.04%) are naturally present, the control experiments performed under a balloon filled with N₂ and open to the atmosphere should be comparable. However, the formation of the symmetrical carbonate **4a** (7%) in entry 6 suggests that more CO₂ was present than is available from the atmosphere. A possible explanation for this observation is the presence of small quantities of Ag₂CO₃ in the Ag₂O, as silver(I) oxide is known to sequester CO₂ from the atmosphere generating Ag₂CO₃ in a reversible reaction (Equation 1).⁴⁵

Additionally, it is possible that the Ag_2O used in the reaction shown in Table 1 is converted to Ag_2CO_3 in the presence of CO_2 under the reaction conditions. The Ag_2CO_3 could then act as a base in the reaction generating an alkoxide and lead to nucleophilic capture of CO_2 as described earlier. However, as previously reported these reactions often require highly polarised solvents to solvate the base, such as DMF²⁴⁻²⁹ or DMSO at 70 °C.³⁰ Teranishi previously established that 5 equivalents of both Ag_2CO_3 and the alkyl halide in DMF were required to generate the corresponding carbonates and only the ether by-product was observed in non-polar CH_2Cl_2 .^{43, 44} The carbonylation of terminal alkynes also showed a strong dependency on solvent, with DMSO affording the best results.⁴¹ As shown in Table 1 however, very high yields of carbonates were achieved under our conditions using CHCl_3 or CH_2Cl_2 as the solvent (*i.e.* entries 1, 2 and 5). As entries 1 and 2 used 25 equivalents of MeOH which could affect the polarity of the solvent, 5 equivalents of MeOH was investigated and still selectively gave the unsymmetrical product **2a** in 95% yield after 3 h (entry 7).

In order to examine the possibility of *in situ* formation and participation of Ag_2CO_3 , the reaction was conducted with Ag_2CO_3 open to the atmosphere, instead of Ag_2O under CO_2 . The reaction was unselective and gave a mixture of products identified by ^1H NMR, and included both the unsymmetrical and symmetrical carbonates **2a** (36%) and **4a** (26%), the methyl ether **3a** (17%) and the corresponding alcohol **5a** (21%) (entry 8, Table 1). Interestingly, when the reaction was conducted with Ag_2CO_3 in the presence of CO_2 , the unsymmetrical carbonate **2a** was selectively generated in 73% with only minor amounts of the symmetrical carbonate **4a** (10%) and alcohol **5a** (17%) (entry 9). In an attempt to replicate the conditions of Teranishi,^{43, 44} 5 equivalents of Ag_2CO_3 open to the air was examined and the major product was the symmetrical carbonate **4a** (69%) and the unsymmetrical carbonate **2a** was the minor product (17%) together with the alcohol **5a** (14%) (entry 10). These results highlight the difference between $\text{Ag}_2\text{O}/\text{CO}_2$ and $\text{Ag}_2\text{CO}_3/\text{CO}_2$ with $\text{Ag}_2\text{CO}_3/\text{air}$ suggesting Ag_2CO_3 is not solely responsible for the alkyl carbonate motif observed in these reactions, although *in situ* generated Ag_2CO_3 which is highly dispersed and more active is still possible and could play an important role in the reaction.

Attempts to perform the reaction with another silver(I) salt, AgCl , failed and only the corresponding chlorinated starting material **7a** was isolated in 87% yield (entry 11, Table 1). Conducting the reaction in MeCN, in which the Cl^- anion is a superior leaving group,⁴⁶ still only gave the chlorinated derivative **7a** (entry 12). Similarly, the reaction with AgF gave the fluorinated starting material **8a** (45%), together with the methyl ether **3a** (55%), determined by ^1H NMR of the crude reaction mixture (entry 13).

The effect of using 0.7 and 0.5 equivalents of silver(I) oxide was investigated and the results are given in Table 2 (entries 2 and 3). Although conversion to the product is still observed with 0.5 equivalents of Ag_2O , the reaction time is longer and unreacted starting materials are also observed.

These preliminary investigations were conducted with *N,N*-dibenzyl β -iodo ethylamine **1a/b** which are thermally stable and

Table 2 Investigation of Ag_2O loading with *N,N*-dibenzyl β -iodo ethylamine **1a**^a

Entry	Ag_2O (equiv.)	Time	Yield (%)		
			1a	2a	3a
1	1.1	35 min.	-	95	-
2	0.7	2.5 h	-	80	-
3^b	0.5	2.5 h	25	67	8

^a Reactions were performed with 25 equiv. MeOH at 20 °C in CHCl_3 under a balloon filled with CO_2 generated from melting dry ice. Yields are of isolated compounds, except where indicated. ^b The ratios were obtained from ^1H NMR of the crude reaction mixture after filtration through Celite®.

easily isolated by column chromatography. ^1H NMR spectroscopy indicated that in CDCl_3 the compounds exist as drawn (**1a/b**) and not as the aziridinium cation that would arise from intramolecular displacement of the iodide.⁴⁷ The alkyl chloride **7a** and fluoride **8a** observed with AgCl and AgF respectively in Table 1, entries 11-13, could be generated by simple $\text{S}_\text{N}2$ displacement or by the aziridinium cation shown in Scheme 3, assisted by the presence of silver in the reaction media.

Scheme 3 Possible formation of alkyl halides **7a** and **8a**

The alkyl iodides **1a/b** also contain a tertiary amine which could act as the base in the reaction and, in addition, are known to sequester CO_2 from the atmosphere.⁴⁸ To investigate this possibility, an unfunctionalised alkyl iodide was examined under the same reaction conditions. 1-Iodoctane **1c** was treated with 1.1 equivalents of Ag_2O , excess MeOH under an atmosphere of CO_2 and gave mixtures of compounds determined by ^1H NMR, including the unsymmetrical carbonate **2c** (Scheme 4).

Scheme 4 Conversion of Oct-I with Ag_2O , CO_2 and MeOH ($\text{R}=\text{C}_8\text{H}_{17}$)

Although the conversion is lower than that previously obtained with the β -iodo ethylamines **1a/b**, even after 16 h, this result still demonstrates that the reaction does not necessarily proceed *via* an aziridinium species. In addition, this result also suggests that the tertiary amine is not necessary for the reaction to proceed, although it does appear to be necessary to obtain high yields. The reaction of unfunctionalised alkyl iodides in this reaction was investigated further and optimised in the study now described.

Table 3 Optimisation of the Ag-mediated capture and functionalisation of CO₂ with alkyl halides^a

Entry	R-X 1	R ¹ -OH (equiv.)	Ag ₂ O (equiv.)	T (°C)	Time (h)	solvent	R-X 1	ROCO ₂ R ¹ 2	R-O-R' 3 (6/9) ^[b]	ROCO ₂ R 4	R-OH 5
1	Oct-I	BnOH (1.5)	1.5	20	18	CHCl ₃	56	22	9	4	9
2	Oct-I	BnOH (1.5)	1.5	45	20	CHCl ₃	31	25	25	5	14
3	Oct-I	BnOH (1.5)	1.1	50	20	CHCl ₃	76	8	5	2	9
4	Oct-I	BnOH (5)	1.1	50	20	CHCl ₃	20	35	22	3	20
5	Oct-I	BnOH (5)	1.5	45	20	CHCl ₃	14	36	24	4	22
6	Oct-I	MeOH (5)	1.1	45	16	CHCl ₃	32	42	10	4	12
7	Oct-I	EtOH (5)	1.1	45	16	CHCl ₃	59	24	7	2	8
8	Oct-I	iPrOH (5)	1.5	45	16	CHCl ₃	16	44	13 (3), 2 (6)	10	15
9	Oct-I	BnOH (1.5)	1.5	20	18	PhMe	69	17	4	2	8
10	Oct-I	BnOH (1.5)	1.5	45	18	PhMe	51	19	11	3	16
11	Oct-I	BnOH (1.5)	1.5	100	18	PhMe	-	11	48 (3), 2 (6), 10 (9)	2	27
12	Oct-I	BnOH (5)	1.5	100	18	PhMe	-	10	47 (3), 11 (9)	1	31
13 ^[c]	Oct-I	BnOH (1.5)	1.5	100	18	PhMe	6	-	71 (3), 2 (6), 14 (9)	-	7
14	Oct-I	BnOH (1.5)	1.5	20	18	MeCN	7	15	3 (3), 2 (6)	7	66
15	Oct-I	BnOH (1.5)	1.5	45	18	MeCN	3	19	5 (3), 1 (6)	6	66
16	Oct-I	BnOH (20)	1.5	20	20	neat	-	55	44	1	-
17	Oct-I	BnOH (20)	1.5	45	4	neat	-	43	40	1	16
18 ^[d]	Oct-I	MeOH (123)	1.1	40	4	neat	-	72	7	2	19
19	Oct-I	iPrOH (30)	1.5	45	5	neat	-	72	13	4	11
20	Oct-I	iPrOH (30)	1.5	45	20	neat	-	75	12	4	9
21	Oct-I	iPrOH (30)	0.5	45	5	neat	45	37	10	2	6
22	Oct-I	iPrOH (30)	0.5	45	20	neat	31	37	23	2	7
23	Hex-Br	iPrOH (30)	1.5	45	20	neat	4	27	4	3	62
24	Hex-Br	BnOH (20)	1.5	45	20	neat	12	12	21 (3), 1 (9)	1	53
25	Hex-Br	BnOH (20)	2	45	16	neat	10	14	22	1	53
26	Hex-Cl	iPrOH (30)	2	45	16	neat	100	-	-	-	-
27	Oct-I	iPrOH (30)	1.5 Ag ₂ CO ₃	45	20	neat	15	35	12 (3), 4 (6)	21	13
28 ^[c]	Oct-I	iPrOH (30)	1.5 Ag ₂ CO ₃	45	20	neat	28	6	31 (3), 3 (6)	7	25
29	Hex-I	BnOH (20)	3 AgCl	45	20	neat	100	-	-	-	-
30	Hex-I	BnOH (20)	3 AgNO ₃	45	20	neat	-	-	54 (3), 46 (9)	-	-
31	Hex-I	BnOH (20)	2.5 AgI	45	16	neat	100	-	-	-	-
			+ 1.0 Ag ₂ O	45	5	neat	-	40	41	2	17

^a The ratios are expressed as % and were obtained from ¹H NMR of the crude reaction mixture after it had been filtered through Celite® and the solvent removed under reduced pressure. All experiments were conducted with 1 mmol of R-X under an atmosphere of CO₂ generated from the sublimation of dry ice, except where indicated. ^b All values are of the unsymmetrical ether 3, unless otherwise stated. ^c Reaction conducted under an atmosphere of N₂. ^d Reaction conducted with 3 mmol Oct-I in 15 mL MeOH.

Optimisation Study

The alkyl halides were chosen to generate non-volatile product mixtures which were analysed by ¹H NMR of the crude reaction mixture, once the silver salts had been removed by filtration and evaporation of the solvent. Various products were identified as shown in Table 3. The ether 3 is the product obtained by direct nucleophilic substitution of the halide 1 by the alcohol, presumably mediated by the silver salt. Similarly, the alcohol 5 is derived from the alkyl halide 1, which is presumably the precursor to the symmetrical carbonate 4 that was also identified in addition to the unsymmetrical carbonate 2.

The reaction was initially investigated with BnOH as the nucleophile and Oct-I using chloroform as the solvent as described in Table 1. Using 1.5 equivalents each of Ag₂O and BnOH at 20 °C gave mostly unreacted starting material 1 (56%) in addition to the unsymmetrical carbonate 2 (22%, entry 1, Table 3). Increasing the temperature to 45 °C led to a greater conversion

of starting material 1 (31%), but did not lead to increased unsymmetrical carbonate 2 (25%, entry 2). Instead both more ether 3 (25%) and alcohol 5 (14%) were observed. Reducing the amount of Ag₂O under similar conditions gave much lower conversions (entry 3), whilst combined with increased amounts of BnOH led to improved conversions, although no selectivity was observed (entry 4). Use of 1.5 equivalents of Ag₂O with 5 equivalents of BnOH did not lead to any noticeable improvement in selectivity in the product distribution (entry 5). Use of different alcohols led to greater selectivity of the unsymmetrical carbonate 2 and although conversions differ greatly, these results demonstrate that both primary and secondary alcohols will react to afford preferentially the unsymmetrical carbonates (entries 6-8).

Using toluene as the solvent, conversions were lower than CHCl₃ at 20 °C (entries 9 and 1, Table 3) and 45 °C (entries 10 and 2). Performing the reaction at 100 °C resulted in complete

conversion of the alkyl iodide **1** and led to the selective formation of the benzyl ether **3** and the corresponding benzoic ester **9** (entries 11 and 12). The benzoic ester **9** was identified by characteristic peaks at 4.32 ppm (t, $J=8.5$ Hz) and 8.05 (d, $J=10.5$ Hz) in the ^1H NMR, which are consistent with the spectroscopic data previously reported for this compound.⁴⁹ The benzoic ester **9** is presumably the result of oxidation of the benzyl ether **3** under the reaction conditions. Ag_2CO_3 can oxidise alcohols⁵⁰ and could be generated *in situ* from Ag_2O and CO_2 ,⁴⁵ however conducting the reaction under N_2 still gave the benzoic ester **9** (14%) in addition to the benzyl ether **3** (71%, entry 13). As expected, neither of the carbonates **2** or **4** were observed in the absence of CO_2 .

Use of MeCN as solvent led to almost complete conversion of the alkyl iodide **1** to the corresponding alcohol **5** (66%, entries 14 and 15, Table 3). This is of interest as, despite its apparent simplicity, methods to transform alkyl halides to the corresponding alcohols often result in elimination or require harsh reaction conditions.^{51, 52} The conversion of alkyl iodides to the corresponding alcohols using silver(I) salts have been previously reported and include Ag_2O ,^{53, 54} Ag_2CO_3 ⁵⁵ and AgBF_4 .⁵²

The highest conversions to the unsymmetrical carbonate **2** were observed when the reactions were performed without additional solvents. Oct-I with 1.5 equivalents of Ag_2O in the presence of an excess of BnOH, as both the reagent and solvent, gave the unsymmetrical carbonate **2** as the major product (55%) and the ether **3** as the minor product (44%) at 20 °C (entry 16, Table 3). Conducting this reaction at 45 °C led to lower selectivity (entry 17). Use of MeOH and i PrOH under similar conditions gave selective conversion to the corresponding unsymmetrical carbonate **2** in 72% (4h, 40 °C, entry 18) and 72% (5h, 45 °C, entry 19), without any significant improvement after 20h (75%, entry 20). Use of 0.5 equivalents of Ag_2O , which still provides stoichiometric Ag(I), only led to diminished conversions as previously observed in Table 2, highlighting the need for an excess of this reagent (entries 21 and 22 in Table 3).

Using our optimised reaction conditions in either i PrOH or BnOH, hexyl bromide gave the corresponding alkyl alcohol **5** preferentially (53-62%) with only low conversion to the carbonates **2** or **4**, even at higher loadings of Ag_2O (entries 23-25, Table 3). This is again of interest as previous methods have required high temperatures,^{51, 56} a two-step procedure,⁵² tin⁵⁷ or HgO ⁵⁸ to convert unactivated alkyl bromides to the corresponding alcohols. No reaction was observed with hexyl chloride presumably due to a lack of reactivity as only starting material was recovered (entry 26).

The silver source was also investigated in this reaction. Since the formation of Ag_2CO_3 is possible *in situ*,⁴⁵ we examined the effects of using pre-formed Ag_2CO_3 in the presence and absence of CO_2 (entries 27 and 28, Table 3). Poor selectivity was observed using Ag_2CO_3 under an atmosphere of CO_2 compared to Ag_2O , which gave 75% unsymmetrical carbonate **2** under the same reaction conditions (compare entries 27 and 20). An increase in the symmetrical carbonate **4** observed with Ag_2CO_3 in entry 27 could be due to simple dialkylation of the silver carbonate motif, as previously reported.⁵⁹ In the absence of CO_2 , Ag_2CO_3 again gave a mixture of compounds but with much less

carbonate **2** or **4** observed (entry 28). This result shows that $\text{Ag}_2\text{O}/\text{CO}_2$ (entry 20) does not afford similar results as $\text{Ag}_2\text{CO}_3/\text{CO}_2$ (entry 27) which is again different to $\text{Ag}_2\text{CO}_3/\text{N}_2$ (entry 28) and consistent with previous observations made in this study.

AgCl under the optimised reaction conditions only gave unreacted starting material **1**, whilst the reaction in the presence of AgNO_3 selectively gave the corresponding ether **3** (entries 29 and 30, Table 3). AgI was also investigated, as it may be a by-product of the Ag_2O reaction and could itself mediate the transformation. In the event however, AgI proved to be unreactive, although upon the subsequent addition of Ag_2O to the reaction, a mixture of products was observed, including the unsymmetrical carbonate **2** (40%, entry 31). This demonstrates that although AgI does not solely mediate the reaction, it does not prevent capture and functionalisation of CO_2 by Ag_2O .

Based on the different results obtained from Ag_2O and Ag_2CO_3 in the presence and absence of CO_2 , it appears that the reaction does not simply proceed *via* initial formation of Ag_2CO_3 which could act as a base and follow the mechanism outlined in Scheme 1. Nor is possible *in situ* formation and subsequent alkylation of Ag_2CO_3 the sole source of the carbonate motif itself.

Isotopic labelling experiments

To demonstrate the ability and utility of the Ag_2O -mediated reaction to capture gaseous CO_2 and transform it into functionalised carbonates, we performed the reaction with ^{13}C -enriched CO_2 (Scheme 5 and Table 4).

Scheme 5 ^{13}C -labelled CO_2 experiments

Various ratios of $^{12}\text{CO}_2$: $^{13}\text{CO}_2$ were generated by adding 3M $\text{HCl}_{(\text{aq})}$ to mixtures of $\text{NaH}^{12}\text{CO}_3$ and $\text{NaH}^{13}\text{CO}_3$,⁶⁰ amounting to 5 equivalents total, and bubbling the $\text{CO}_{2(\text{g})}$ evolved directly through the reaction mixture and into an empty balloon as a reservoir (Scheme 5 and Table 4). The ratios of the ^{12}C and ^{13}C NaHCO_3 were determined using a 5-figure balance. After 4h, the reaction mixture was filtered to remove the silver salts and evaporated carefully under reduced pressure to afford the hexyl methyl carbonate **2d** without the need for further purification.

The yields of the methyl carbonate vary between 60% and 70% (entries 1-5, Table 4). This variation in yield is a reflection of the heterogeneity of the reaction, as the reactants are in three different phases; gas (CO_2), liquid (solution of Hex-I **1d** in MeOH) and solid (insoluble Ag_2O). It is therefore susceptible to factors such as the rate of stirring. In addition, the variation in yield may also be due to the volatility of the carbonate product **2d**. The yields 60-70% are however in good agreement with the

Table 4 Synthesis and analysis of ^{13}C -labelled carbonates **2d**^a

Entry	Yield (%) ^b	Measured ratio of NaHCO_3 ^c		Observed ratio ^{13}C NMR ^d		Observed ratio HRMS ^e	
		^{12}C	^{13}C	^{12}C	^{13}C	^{12}C	^{13}C
1	63	100	0	100	0	100	0
2	68	75	25	74.2±1.7	25.8±1.7	73.6	26.4
3	68	50	50	50.4±1.2	49.6±1.2	49.7	50.3
4	70	25	75	28.0±2.3	72.0±2.3	28.3	71.7
5	60	0	100	2.1±1.8	97.9±1.8	2.9	97.1

^a All reactions were performed by adding 3M $\text{HCl}_{(\text{aq})}$ to NaHCO_3 (5 equiv.) and passing the CO_2 gas generated through a rapidly stirred suspension of Hex-I (1 equiv.) and Ag_2O (1.2 equiv.) in MeOH. The reaction was then rapidly stirred at 40 °C for 4h. ^b Yield of **2d** after filtration and careful evaporation under reduced pressure. ^c Ratio of the $\text{NaH}^{12}\text{CO}_3$ (99% ^{12}C) and $\text{NaH}^{13}\text{CO}_3$ (99% ^{13}C). ^d Average of ratios obtained from a comparison of the C=O peak with each of the aliphatic carbon signals (seven calculations). ^e Ratio based on MNa^+ (ESI⁺). ^d and ^e see ESI† for calculations.

conversions observed in the optimisation study, in which Oct-I gave the corresponding unsymmetrical carbonate **2** in 75% yield by ^1H NMR in comparable reaction conditions (entry 20, Table 3). Since the product **2d** was obtained pure after evaporation of the solvent, the remainder of the mass balance must have been composed of volatile materials such as the competing hexylmethyl ether **3d** (b.p 117-120 °C at 763 mmHg),⁶¹ which is more volatile than the hexylmethyl carbonate product **2d** (b.p 75-76 °C at 20 mmHg).⁶²

The products were analysed by standard ^{13}C NMR and High Resolution Mass Spectroscopy. The C=O peak in the ^{13}C NMR was indicative of ^{13}C incorporation and from calculations shown in the Electronic Supplementary Information (ESI†), the ratios of ^{12}C : ^{13}C could be determined based on integration of the carbonyl peak with respect to each of the aliphatic peaks. The calculations take into account the natural abundance of ^{13}C and also the different relaxation rates for different peaks. It is interesting to note that the product obtained from 100% $\text{NaH}^{13}\text{CO}_3$ showed additional coupling in both the ^1H and ^{13}C NMR spectra, due to the presence of the ^{13}C and consistent with similar ^{13}C -carbonyl-labelled carbonates.^{63, 64}

Similarly, a ratio between the ^{12}C and ^{13}C products could also be determined from integration of the peaks corresponding to MNa^+ by HRMS and are given in Table 4. The calculations again consider the natural abundance of ^{13}C and are fully described in the ESI†. The results shown in Table 4 demonstrate that it is indeed possible to generate ^{13}C -labelled carbonates specifically labelled at the carbonyl group from $^{13}\text{CO}_2$ under mild reaction conditions and without specialist equipment. The results also show that the extent of isotopic labelling can be accurately controlled and determined by standard ^{13}C NMR and mass spectroscopy, using the calculations shown in the ESI†, which are in excellent agreement with each other and with the expected ratios in all cases.

No effort was made to purge the system of residual natural atmospheric CO_2 before generating and introducing the $^{12}\text{CO}_2$: $^{13}\text{CO}_2$ mixtures, which had no noticeable effect as theoretical and observed ratios were consistent (entries 1-5, Table 4). When the reaction shown in entry 3 was purged with N_2 prior to generation of CO_2 , there was no difference in the isotopic ratios observed by ^{13}C NMR (spectra of purged 50/50 reaction given in the ESI†). Further investigations showed that when the

reaction shown in entry 5 was performed with Ag_2CO_3 in place of Ag_2O , a mixture of products was obtained with little selectivity (result not shown, but spectra given in the ESI†). The theoretical maximum ^{13}C incorporation using 100% $\text{NaH}^{13}\text{CO}_3$ is actually 99% as this was the isotopic purity of the starting material (Certificate of Analysis shown in the ESI†).⁶⁰ Our results are very close to this theoretical maximum and are in excellent agreement with each other (97.9±1.8% NMR and 97.1% HRMS, entry 5).

This transformation offers convenient access to specifically labelled carbonates in high purity and good yields. This is of great interest as there are very few methods to generate similar compounds,⁶⁴⁻⁶⁷ which have a wide range of applications including biosynthesis and metabolism. This methodology could be directly applied to make tracers for positron emission tomography (PET) imaging using $^{11}\text{CO}_2$,⁶⁸ which complements current technologies that employ ^{11}CO to generate amides.^{69, 70}

Conclusion

Based on the different results obtained from Ag_2O and Ag_2CO_3 in the presence and absence of CO_2 , it appears that the reaction does not simply proceed *via* the initial formation of Ag_2CO_3 , which could act as a base or source of the alkyl carbonate motif itself. It is therefore worthy of note that the reaction described herein proceeds without the need of an external base and may find applications with base-sensitive substrates. It should also be noted that CO_2 fixation was achieved by an inorganic silver(I) salt and may be amenable to heterogeneous catalysis.

The Ag_2O -mediated reaction is able to capture and functionalise CO_2 to generate synthetically useful unsymmetrical carbonates under mild reaction conditions and ambient temperatures, without the need for specialised equipment. The formation of ^{13}C -carbonyl-labelled dialkyl carbonates exemplifies the ability to sequester and functionalise gaseous CO_2 with Ag_2O at atmospheric pressure and 40 °C without the need of an external base. The ^{13}C -carbonyl-labelled carbonates were readily generated with exquisite control of the isotopic purity under mild reaction conditions in good yields using standard equipment.

Experimental Section

Full experimental data including ^1H and ^{13}C NMR spectra are provided in the Electronic Supplementary Information (ESI†). Below are representative experimental procedures for key transformations. $\text{CO}_{2(\text{g})}$ was simply generated by allowing commercially available dry ice ($\text{CO}_{2(\text{s})}$) to sublime at room temperature in a stoppered flask fitted with an empty balloon. The balloon would gradually fill with CO_2 gas which was used directly in the CO_2 reactions.

2-*N,N*-Dibenzylaminoethyl methyl carbonate (**2a**)

N,N-Dibenzylamino-2-iodoethane **1a** (50 mg, 0.14 mmol) was dissolved in CHCl_3 (2 mL) and CO_2 (1 balloon) was bubbled through. MeOH (0.14 mL, 3.5 mmol, 25 equiv.) was added, followed by Ag_2O (37 mg, 0.16 mmol, 1.1 equiv.) and the reaction vigorously stirred under an atmosphere of CO_2 at room temperature for 35 mins. The reaction mixture was filtered through a cotton wool and silica plug and washed with CHCl_3 (10 mL) and EtOAc (10 mL). The solvent was removed under

reduced pressure to give, without the need for further purification, the unsymmetrical carbonate **2a** (40 mg, 95% yield) as a colourless oil. Full characterisation data is provided in the ESI†.

5 General Synthetic Procedure for ¹³C-labelled experiments (Table 4, Scheme 5)

The desired mixture of NaHCO_{3(s)} was accurately weighted and placed in a sealed 5 mL round-bottomed flask, fitted with a cannula which was positioned in the air-space above the reaction mixture. The other end of the cannula was positioned in the reaction mixture of a separate and sealed round-bottomed flask which contained a rapidly stirred suspension of the alkyl iodide, Ag₂O and MeOH at room temperature. This flask was also fitted with an empty balloon to act as a reservoir of the CO_{2(g)} produced. The addition of 3M HCl_(aq) to the first flask containing the NaHCO_{3(s)} generated CO_{2(g)} which passed through the cannula and into the reaction mixture in the second flask and into the balloon reservoir. Once the bubbling had ceased and no more NaHCO_{3(s)} was evident, the cannula was removed from the reaction mixture in the second flask and the reaction heated to 40 °C for 4 hours under the balloon filled with CO₂. The reaction was filtered through filter paper and cotton wool, washed with MeOH and the solvent carefully removed under reduced pressure to afford carbonate **2d**. Full experimental and characterisation data is provided in the ESI†.

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