RSC Mechanochemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: C. Bozdemir, M. E. Çelik, M. Mart, A. Alemdar, A. Baydar and C. Dengiz, *RSC Mechanochem.*, 2026, DOI: 10.1039/D6MR00048G.

View Article Online
DOI: 10.1039/D6MR00048G

ARTICLE

Liquid-Assisted Ball-Milling Synthesis of Organic Carbonates as Aroma Compounds

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Can Bozdemir,[a] Mehmet Efe Çelik,[a] Mehmet Mart,[a] Aydın Alemdar,[b] Ahmet Baydar,[b] and Cagatay Dengiz[a]*

A new approach based on ball milling is introduced as an efficient and greener alternative to conventional solution-based methods for the synthesis of carbonate compounds, which typically require toxic solvents (e.g., dichloromethane) and bases such as pyridine. Following an initial proof-of-concept, the scalability of the method was demonstrated on gram scale using two representative reactions, including the synthesis of the fragrance molecule liffarome and the reaction of vanillin with isobutyl chloroformate, affording the desired products in 42% and 74% yield, respectively. Using this solvent-free methodology, a total of nine new carbonate-based aroma compounds were synthesized and fully characterized. Their olfactory properties were evaluated by an expert panel, revealing diverse and, in some cases, unexpected odor profiles, which were classified into floral, spicy, fruity, green, and gourmand categories. A comprehensive comparison with traditional and water-based methods showed that ball milling generally provides superior or comparable yields (up to 84%) while avoiding hazardous solvents. Green metrics further highlight the advantages of the ball-mill approach: atom economy values were higher for ball milling (72.2–78.9%) compared to the traditional method (63.2–71.2%), similarly real atom economy reached up to 0.580 for ball milling compared to 0.151 for the traditional method. Notably, the process mass intensity (PMI) was as low as 1.73 for ball milling, making it nearly seven times more resource-efficient than the conventional approach (PMI = 11.96). Furthermore, analysis of the liquid-assisted grinding (LAG) parameter (η) revealed that higher liquid-to-solid ratios, achieved in the absence of solid auxiliaries, lead to improved reaction efficiency. Overall, this study demonstrates that ball milling offers a practical, scalable, and sustainable strategy for the synthesis of fragrance-related carbonate compounds, while also enabling access to structurally diverse molecules with unique olfactory properties.

Introduction

Although the chemical industry plays a significant role in our society,[1] yet its operations have a considerable environmental impact, ranking as the third-largest source of greenhouse gas emissions and the leading industrial consumer of fossil fuels.[2,3] Accounting for approximately 5% of global CO_2 emissions, the chemical industry is a key sector in achieving net-zero targets.[4] Given the environmental impacts of this giant industry, it is inevitable for the chemical industry to transition to more sustainable production methods and the development of eco-friendly products to safeguard our planet and nature and mitigate the effects of climate change.[5] The Fragrance industry, a sub-branch of the chemical industry, is one of the key sectors involved in many aspects of daily life. From perfumes to fabric softeners, dishwashing detergents and even toilet paper, fragrances fall into various categories to enhance the sensory experience.[6] Considering that each perfume consist of hundreds of natural and synthetic chemicals and the fragrance ingredient market is projected to reach USD 16.1 billion by 2027, the significance of green synthesis methods for a sustainable future is evident. Keeping these numbers in mind, various green techniques are being developed: biotechnology is being incorporated into fragrance synthesis to replace classical production of both natural and synthetic ingredients,[7] green catalysts are being employed to enhance environmental sustainability,[8] and the regular use of flow reactors is now recognized as essential for sustainable production.[9] Microwave-assisted organic synthesis of fragrances is another green synthetic approach[10] that has been attracting increasing attention with each passing day.[11,12] The search for sustainable production methods and highly biodegradable fragrance ingredients[13] led our research to develop a ball mill protocol for synthesizing new carbonate-structured fragrance ingredient candidates, in line with both research objectives. At this point, it is notable that mechanochemistry, a method fully compatible with green chemistry principles,[14] is scarcely used in the synthesis of fragrance ingredients, with only a few partially relevant examples in the literature.[15,16] Although its use in fragrance chemistry is limited, green applications in the synthesis of materials like nanomaterials,[17] pharmaceuticals,[18] dyes,[19] and polymers[20] highlight the potential of this method. Organic carbonates, known for their high solubility in nature and used as green solvents[21] as an alternative to flammable/volatile organic compounds are also used as

[a] Department of Chemistry, Middle East Technical University, 06800 Ankara, Türkiye
[b] R&D Center, MG International Fragrance Company 41400, Kocaeli, Türkiye

fragrance ingredients. Figure 1 provides an overview of the odor profiles for selected examples of carbonate-based fragrance ingredients. Compounds **I**[22] and **II**[23] are among the most well-known carbonate-structured fragrance ingredients, characterized by their prominent violet leaf scent. Compound **III**[24] serves as a modifier for jasmine fragrances, adding a sweet and rich base note. Compound **IV**[25] contributes rosy and fruity accents to various fragrance compositions, while compound **V**[26] imparts a rosy and spicy character to scents.

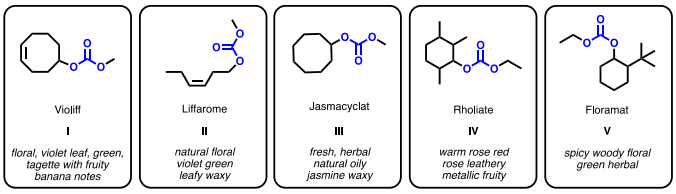


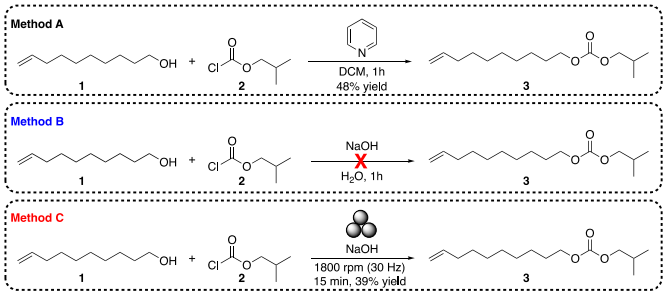
Figure 1. Representative carbonate-structured fragrance ingredients highlighting their distinct olfactory properties.

While organic carbonates are often described, as mentioned before, as green solvents, their industrial synthesis, particularly of the linear variants, relies heavily on the use of highly toxic phosgene gas, which raises significant concerns about the environmental sustainability of these processes.[27] In general, the synthesis of linear carbonates involves methods such as phosgenation,[28] the addition of CO_2 to acetals,[29] and carbonylative oxidation,[30] while cyclic carbonates are typically obtained through the addition of CO_2 to diols and epoxides, representing well-established CO_2 fixation strategies, although many such methodologies still face practical limitations such as the requirement for high pressure, specialized catalysts, or limited substrate scope.[31,32] Another well-established method, frequently employed at the laboratory scale for the high-yield synthesis of carbonates, involves the reaction between alkyl chloroformates and alcohols.[33] However, this approach poses significant environmental challenges due to the production of HCl gas, the use of weak bases such as pyridine and triethylamine for its neutralization, and the dependence on inert solvents such as dichloromethane (DCM) and tetrahydrofuran (THF) to sustain the reaction. Given the extremely low odor thresholds and unpleasant odors of pyridine and triethylamine, it is anticipated that even trace amounts of residues remaining after the reaction could potentially alter the odor profiles of the target aroma compounds.[34] Herein, 9 new carbonate-based fragrance ingredient candidates were synthesized using the ball milling strategy, which has seen limited application in fragrance chemistry. This method eliminates the need for toxic solvents and bases with low odor thresholds, and their odor profiles were extensively analyzed. This study is considered a pioneering effort in the fragrance industry and is expected to encourage greater adoption of the ball milling technique in the near future.

Results and discussion

Optimization studies.

Our study began with a comparative analysis of two distinct methods[35–37] from the literature for synthesizing organic carbonates, utilizing alcohols and alkylchloroformates as well as a ball milling approach (Methods A, B, and C) (Scheme 1). The commercially available substrates selected for the optimization reactions were dec-9-en-1-ol (**1**) and isobutyl chloroformate (**2**). By following Method A,[36,37] the target carbonate **3** was obtained with a yield of 48% after conducting the reaction at room temperature in the presence of DCM and pyridine. In the following step, we tested the synthesis of the target products based on a green synthesis from the literature,[35] which involves phenol derivatives and alkyl chloroformates in the presence of water and NaOH, without generating toxic by-products. Unfortunately, under these conditions (Method B), the substrate containing the primary alcohol **1** did not react with the chloroformate **2**. We attribute this result to the greater acidity of phenol derivatives, which react with NaOH to generate more nucleophilic phenoxide ions. Since primary alcohols cannot be deprotonated by NaOH, the lack of reaction is considered normal. Following the ball milling optimizations, the reaction will be tested with all substrates, and this initial observation will be further explored.



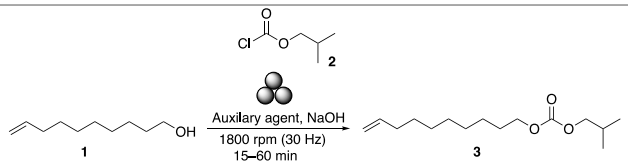
Scheme 1. Comparison of three methods for the synthesis of carbonate **3**: (Method A) Traditional alcohol-alkyl chloroformate reaction conducted in DCM with pyridine as the base, (Method B) alcohol-alkyl chloroformate reaction performed in water with NaOH as the base, and (Method C) ball milling approach used in this study, highlighting a solvent-free strategy.

In the trial for the final method (Method C), the substrates and NaOH were milled at 30 Hz under ambient conditions for 15 minutes, yielding the target carbonate **3** with an isolated yield of 39% (Table 1). Due to both starting materials being liquids, it was important to demonstrate that the reaction proceeded via ball milling. For this purpose, identical quantities of substrates and NaOH were mixed neat for one hour as a parallel experiment. As anticipated, only trace amounts of the product were formed, confirming that the reaction occurred through ball milling process. To refine the initial outcomes, the optimization of reaction conditions was carried out. Parameters such as reaction time, the type of auxiliary, and its amount were evaluated. All reactions took place under ambient conditions, and yields were determined from the isolated compound **3**. In the first stage, reaction times were systematically extended without the use of any auxiliary, and the resulting changes in

View Article Online
DOI: 10.1039/D5MR00048C

yields were analyzed (Entries 1–3). Under these conditions, increasing the reaction time from 15 to 30 minutes led to a yield improvement from 39% to 58%. Further extending the reaction time to 60 minutes increased the yield to 84%. When one or more of the reagents in a reaction are liquids, auxiliary agents such as silica, alumina, and/or inorganic salts are typically used to enhance reaction efficiency.[38] The presence of liquids often leads to the formation of a gum-like structure during ball milling, which restricts mass and energy transfer. Since both substrates were liquids in our case, the reactions were repeated in the presence of auxiliary agents. When selecting auxiliary agents, NaCl and neutral Al_2O_3 were chosen for their abundance and relatively eco-friendly characteristics, as they are derived from natural sources. Another reason for choosing NaCl as an auxiliary agent is that if the reactions are scaled up for carbonate synthesis, the NaCl produced as a byproduct could also be used as an auxiliary agent in the reactions, promoting a cyclical process. The initial 15-minute experiments with neutral Al_2O_3 revealed that increasing the auxiliary agent quantity from 1.5 g to 3.0 g raised the yields from 6% to 18% (Entries 4 and 5). In 30-minute experiments using 1.5 g to 3.0 g of Al_2O_3, a similar trend was noted, though the yield improvement was minimal compared to the 15-minute reactions (Entries 6 and 7). The results show that reactions without an auxiliary agent produced substantially higher yields than those conducted with Al_2O_3 as an auxiliary agent.

Table 1. Optimization of reaction conditions for the ball milling synthesis of carbonate **3**.



Entry[a]	*Auxilary Type*	*Auxilary Amount (g)*	*Time (min.)*	*Yield (%)*[b]
1	–	–	15	39%
2	–	–	30	58%
3	–	–	60	84%
4	Al_2O_3 (neutral)	1.5 g	15	6%
5	Al_2O_3 (neutral)	3.0 g	15	18%
6	Al_2O_3 (neutral)	1.5 g	30	10%
7	Al_2O_3 (neutral)	3.0 g	30	22%
8	NaCl	1.5 g	15	71%
9	NaCl	3.0 g	15	62%
10	NaCl	1.5 g	30	78%
11	NaCl	3.0 g	30	74%

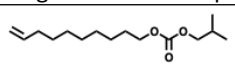
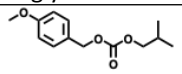
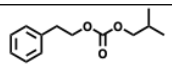
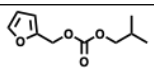
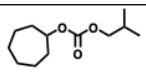
[a]Reactions were conducted under ambient conditions. **1** (1 equiv.), NaOH (1.3 equiv.), and **2** (1.2 equiv.) [b]Yields were determined based on isolated product.

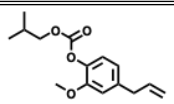
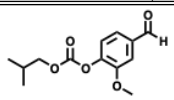
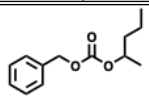
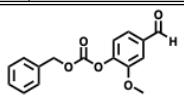
We observed interesting results in our experiments using NaCl as an auxiliary agent. In both the 15-minute and 30-minute reactions, increasing the amount of NaCl from 1.5 grams to 3 grams led to a slight decrease in yields (from 71% to 62% for 15 minutes and from 78% to 74% for 30 minutes, Entries 8–11). We presume that an excess of NaCl could raise viscosity or cause clumping during the reaction, hindering the effective interaction of reactants and causing a decrease in yield. The strong yield increase observed with longer reaction times in reactions without auxiliary agents was not seen in those with auxiliary agents. As a result, we decided to set the reaction time to 30 minutes for reactions with auxiliary agents on different substrates. This decision was made because the minimal yield increase with longer reaction times would make the experiments less energy-efficient, moving them away from green synthesis principles. Consequently, five different reaction conditions (Method A, Method B, Method C.1–C.3, Entries 3, 7, and 10) were explored for each substrate to be tested in the next stage (Table 2). In this section of the study, the reactions of primary/secondary alcohols and phenol derivatives with two different alkyl chloroformates (isobutyl and benzyl chloroformate) are investigated, resulting in the synthesis of nine new carbonate-based potential fragrance ingredients **3**–**11**. When examining the reactions between primary alcohols and isobutyl chloroformate, the target products **3**–**6** were synthesized. A comparison of the traditional Method A (41–74%) with the ball mill-based Method C.1 (58–84%) revealed consistent yield improvements across all substrates, demonstrating that the ball mill approach is a significant alternative to the traditional method for reactions involving primary alcohols. Unfortunately, reactions conducted in water with primary alcohols (Method B) resulted in low yields (0–28%) and did not provide a viable alternative to the other methods. In syntheses involving primary alcohols with auxiliary agents, Methods C.2 and C.3 generally did not demonstrate significant advantages over Method C.1. However, when reactions were conducted following Method C.3 in the presence of 1.5 g of NaCl, the yields achieved were closer to those obtained with Method C.1. In the synthesis of carbonates **7** and **10**, where secondary alcohols were used as substrates, traditional methods (Method A) demonstrated better performance compared to other approaches. In ball milling, the reaction proceeds through mechanical activation and effective collision between reactants; however, steric hindrance associated with secondary alcohols can reduce accessibility to the reagent surface, leading to less efficient interactions and slower reaction rates. Overall, the efficiency of the method is substrate-dependent and may be significantly reduced for secondary alcohols. The results obtained in the synthesis of carbonates **8**, **9**, and **11**, using phenol derivatives as substrates, were even more remarkable. As an alternative to the traditional method, Method B, conducted in water with NaOH, yielded the target products in comparable yields with Method A. These findings were consistent with our previous discussion. More acidic phenols, compared to primary and secondary alcohols, generate phenoxide ions in the reaction medium, facilitating more efficient reactions. In ball milling experiments following

View Article Online
DOI: 10.1039/D6MR00040C

Method C.1, the yields for compounds **8** and **9** were slightly lower compared to Method A, while a significant increase in yield was observed for compound **11**. Method C.2, which used neutral Al_2O_3 as an auxiliary agent, resulted in very low yields across the entire series, whereas Method C.3, which involved NaCl, did not surpass Method C.1 except for compound **8** but still provided yields close to those of Method C.1. These results demonstrate that the ball milling method (Method C.1) offers a significant alternative to the traditional Method A and suggests that target reactions can be carried out under eco-friendly conditions. Although the auxiliary agents neutral Al_2O_3 and NaCl did not lead to yield increases in ball milling, NaCl was found to offer a significant advantage over Al_2O_3. Furthermore, it was shown that, in the reaction of phenol derivatives with chloroformates, both ball milling methods and reactions in aqueous NaOH could serve as alternatives to the traditional Method A. To ensure complete scavenging of the generated HCl and to drive the reaction to completion, a slight excess of NaOH (1.3 equiv.) was employed in Methods B and C.1–C.3. These findings are crucial as they highlight the feasibility of methods that do not rely on toxic reagents such as pyridine and DCM in organic carbonate synthesis. To evaluate the gram-scale applicability of the developed process, two compounds, Liffarome (**II**, a commercial fragrance molecule, see Figure 1) and compound **9**, were tested and isolated in 42% and 74% yields, respectively (see the Scale-Up Experiments Section in the SI for further details). Although the polytetrafluoroethylene (PTFE)-based conditions were successfully optimized at small scale to obtain sufficient quantities for olfactory evaluations, these parameters were not directly transferable to gram-scale synthesis, and therefore gram-scale reactions required separate re-optimization using stainless steel milling equipment.

Table 2. Synthesis of various carbonate derivatives using five different methods: Method A,[a] Method B,[b] Method C.1,[c] Method C.2,[d] and Method C.3,[e] along with the corresponding yields.

	 **3**	 **4**	 **5**	 **6**	 **7**
Method A	48%	50%	74%	41%	68%
Method B	no reaction	1%	4%	28%	17%
Method C.1	84%	58%	74%	76%	30%
Method C.2	22%	4%	4%	16%	10%
Method C.3	78%	61%	55%	71%	24%

	 **8**	 **9**	 **10**	 **11**
Method A	87%	68%	30%	28%
Method B	80%	63%	6%	29%
Method C.1	70%	68%	13%	60%
Method C.2	31%	9%	6%	9%
Method C.3	78%	64%	19%	22%

[a]**Method A**: alcohol (1 equiv), chloroformate (1.2 equiv), pyridine (1.3 equiv.), DCM (5 mL); [b]**Method B**: alcohol (1 equiv), chloroformate (1.2 equiv), NaOH (1.3 equiv.), H_2O (5 mL); [c]**Method C.1**: ball milling (60 min, 30 Hz), alcohol (1 equiv), chloroformate (1.2 equiv), NaOH (1.3 equiv.); [d]**Method C.2**: ball milling (30 min, 30 Hz), alcohol (1 equiv), chloroformate (1.2 equiv), NaOH (1.3 equiv.), Al_2O_3 (neutral, 3.0 g); [e]**Method C.3**: ball milling (30 min, 30 Hz), alcohol (1 equiv), chloroformate (1.2 equiv), NaOH (1.3 equiv.), NaCl (1.5 g).

The chemical structures of all carbonates were confirmed through ^{1}H NMR, ^{13}C NMR, IR, and HRMS analyses. The protons on the carbon atoms adjacent to the oxygen atoms in the carbonate group typically give signals over 3.5 ppm due to the electron-withdrawing nature of carbonates. ^{13}C NMR is generally more effective for characterization purposes. The carbonate carbonyl group signals are consistently observed in the range of 150–160 ppm across all structures. Carbons neighbouring the oxygen atoms in the carbonate group exhibit signals above 60 ppm in ^{13}C NMR. Additionally, all IR spectra feature strong absorption bands between 1730–1760 cm^{-1}, corresponding to the stretching vibrations of the carbonate carbonyl groups. HRMS analysis shows that the calculated mass values align perfectly with the measured values, further confirming the structures of the synthesized carbonates. All spectra (^{1}H NMR, ^{13}C NMR, IR, and HRMS) are included in the supporting information.

Evaluation of Liquid-Assisted Grinding (LAG) Parameter

To understand the influence of liquid content on reaction efficiency, we evaluated the LAG parameter [liquid-to-solid ratio (η, in mL/g)] for compounds **3–11** under three different methods: C1 (no solid auxiliary), C2 (with neutral Al_2O_3, 3.0 g), and C3 (with NaCl, 1.5 g) (Table S1 in the SI).[39] Method C1

View Article Online
DOI: 10.1039/D6MR00048G

consistently provided the highest η values, ranging from 0.765 to 6.481 mL/g depending on the compound, reflecting the purely liquid nature of the reactants and the absence of solid diluents. This higher η leads to paste formation in the milling jar, which correlates with superior reaction efficiency in ball milling. For example, compound **3** under Method C1 reached an η of 6.481 mL/g, whereas Methods C2 and C3 showed drastically lower η values of 0.071 and 0.140 mL/g, respectively. A similar trend was observed for compounds **4–11**. Compounds with inherently lower η values under C1, such as **9** (0.765 mL/g) and **11** (0.843 mL/g), still outperformed the corresponding C2 and C3 methods, highlighting the importance of minimizing solid diluents. In Methods C2 and C3, the inclusion of Al_2O_3 or NaCl as solid auxiliaries significantly reduced the effective liquid-to-solid ratio, reflecting the lower mobility of the reaction mixture inside the milling jar. This decreased η was associated with slower mass transfer and reduced reaction efficiency. For instance, for compound **10**, η dropped from 5.378 mL/g (C1) to 0.104 mL/g (C2) and 0.204 mL/g (C3). Overall, these observations clearly indicate that maximizing the liquid content relative to solids in the milling jar (as in Method C1) enhances the efficiency. The results highlight that, for the reactions studied, the optimal balance between liquid content and mechanical energy input is achieved under solvent-minimized but non-diluted conditions.

Olfactory properties

The new organic carbonates were evaluated by MG International Fragrance Company and their expert team. The odor profiles were analyzed by an R&D executive, a master perfumer, two junior perfumers, two R&D managers, and a perfumer's assistant. In the fragrance industry, it is common practice to combine two fragrance ingredients into a single structure, producing a final compound that embodies the olfactory traits of both starting materials. For example, the reaction between hydroxycitronellal and methyl anthranilate forms a Schiff base that merges the lily-of-the-valley scent from the hydroxycitronellal component with the orange blossom nuances of the methyl anthranilate moiety.[40,41] Similarly, the new aroma compounds introduced in this research are anticipated to exhibit dual olfactory characteristics derived from their precursors, with the potential to interact with distinct olfactory receptors from each part of the molecule. Figure 2 categorizes the carbonates according to their distinctive odor profiles.

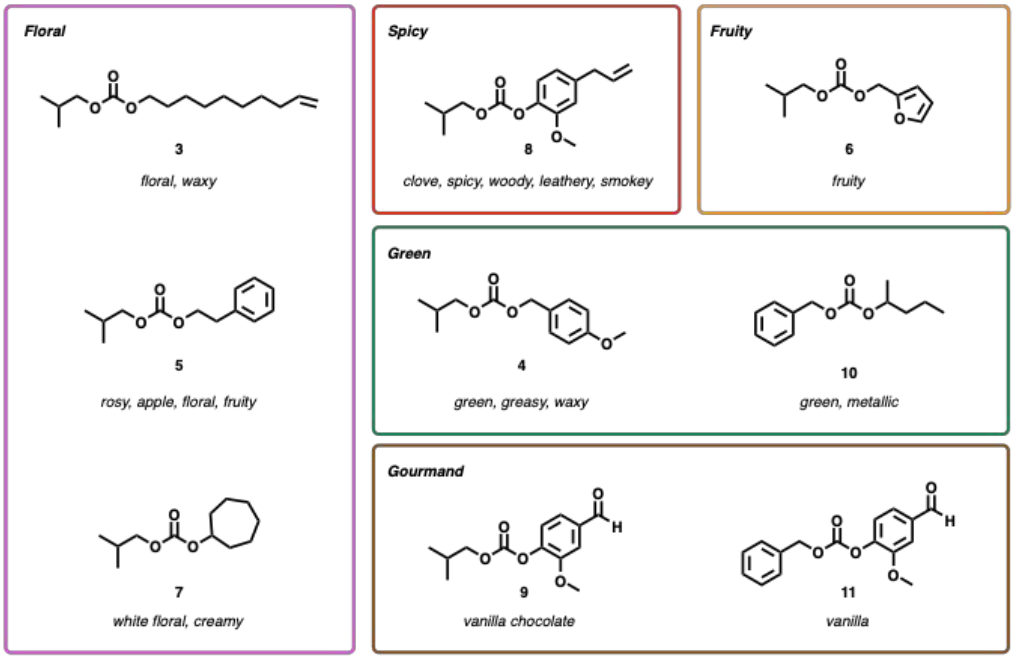


Figure 2. Evaluation of the olfactory properties of the synthesized organic carbonates **3–11**.

The synthesized molecules exhibited diverse olfactory profiles, often deviating from their predicted characteristics. Compound **3** was expected to feature a floral, waxy profile from its 9-decen-1-ol-like side, paired with fruity notes from the isobutyl acetate-like portion; however, it dominantly reflected floral, waxy traits without the anticipated fruity aspects. Compound **4**, anticipated to deliver an anisic scent from its anisyl acetate-like side combined with fruity notes, instead showed green, greasy, and waxy characteristics. Compound **5** successfully presented the expected rosy, floral scent from its phenylethyl acetate-like portion, complemented by green apple-like fruity nuances. Compound **6**, predicted to produce a complex banana-like aroma from the shared banana-like notes of furfuryl acetate and isobutyl acetate, resulted in a general fruity odor lacking a distinct banana note. Compound **7** diverged from its faint cycloheptanol and fruity isobutyl acetate-like components, developing a creamy, white floral scent. Compound **8**, expected to combine a spicy eugenyl acetate-like aroma with fruity notes, delivered a clove-like scent with woody, leathery, and smoky undertones, resembling the IFRA-regulated ingredient "Isoeugenol."

View Article Online
DOI: 10.1039/D6MR00048G

Compound **9** achieved a vanilla and milky chocolate-like odor profile, aligning with expectations of a vanilla scent from its vanillyl acetate-like side and fruity undertones. Compound **10**, anticipated to blend jasmine-like notes from its benzyl acetate-like portion with green notes from its 2-pentyl acetate-like side, instead revealed a predominantly green and weedy profile, lacking the expected jasmine character. Compound **11**, designed to offer a complex vanilla scent by combining vanillyl acetate-like and creamy banana-like benzyl acetate-like traits, showed faint vanilla-like characteristics. Several factors could explain why some molecules did not exhibit the expected odor characteristics. For **3**, **8**, and **10**, the predominance of one-sided odors may result from the molecules' tendency to bind preferentially from one side, leading to an imbalance in the olfactory profile. In compounds **4** and **7**, the loss of both odor characteristics from the starting ingredients could be attributed to a reduction in receptor specificity in the final molecules, potentially caused by steric hindrance. For **6**, the general fruity scent observed might stem from the molecule activating more than two olfactory receptors, generating multiple olfactory signals that overshadowed or eliminated the anticipated banana-like aroma. The chocolate-like scent of **9** may result from the attachment of an isobutyl group to an aromatic ring, a phenomenon also observed in other fragrance ingredients like vanillyl isobutyrate and isobutyl pyridine, which similarly exhibit chocolate-like effects. Compounds **5** and **11** displayed the expected odor profiles, supporting the initial hypotheses. These findings emphasize the need for further research to better understand the complex interactions between molecules and olfactory receptors. Such insights could enable the precise design of carbonate-structured aroma compounds with more targeted and predictable odor profiles.

Green metrics

To compare the methods used in the synthesis of carbonate-based aroma compounds **3**–**11** and quantitatively determine which process is greener, 3 different green metric parameters [atom economy (AE), real atom economy (RAE), and process mass intensity (PMI)] were calculated and analyzed for three different cases: Methods A, B, and C.1 (Table 3).[42] In Method A, a different base (pyridine) is used compared to Methods B and C1, leading to significant differences in the atom economy values; Method A shows AE values in the range of 63.2–71.2%. In contrast, Methods B and C1 utilize the same reagents and equivalents, resulting in consistent AE values in the range of 72.2–78.9%. Changing the base to NaOH slightly increases the obtained AE values. These findings demonstrate that the synthesis of carbonate-based molecules via alcohol-chloroformate reactions approaches optimal resource utilization, making the process highly atom-efficient. In terms of RAE, Method C.1 demonstrates higher efficiency for all compounds compared to Methods A and B. With an optimal RAE value of 1, the highest result for Method C.1 is 0.580, whereas the highest value for the traditional Method A is 0.151. This indicates that Method C.1 is over four times more efficient at converting raw materials into products. These findings confirm the superior performance of Method C.1 over Method A in terms of real atom economy. PMI results indicate that Method C.1 exhibits superior resource efficiency compared to the traditional Method A. all PMI values for Method C.1 are better than those for Method A. Among the entire series, compound **3** demonstrates the best PMI value of 1.73, making it almost seven times more resource-efficient than the traditional Method A (PMI for compound **3**: 11.96). These findings highlight the effectiveness of ball mill Method C.1 in minimizing material input while maximizing product output in carbonate synthesis. Although the developed methodology does not directly compete with state-of-the-art CO_2 fixation strategies in terms of overall sustainability metrics, it remains a valuable complementary approach when the practical limitations of such systems are considered. In particular, many CO_2-based carbonate syntheses require high pressure conditions and specialized catalysts, which can limit their operational simplicity and accessibility.[31] In contrast, the present method proceeds under mild conditions without the need for external catalysts, solvents, or amine bases, thereby offering a more straightforward and operationally convenient alternative that reduces reliance on additional reagents commonly employed in conventional protocols. Reported green metrics correspond to reaction-based metrics only; solvents and work-up materials are not included. Within the scope of this study, the sole purpose was the comparison of three different methodologies under identical conditions. However, for comparisons with different reactions or literature methods, solvents and work-up procedures should also be considered, which would inevitably increase the PMI values.

Table 3. Comparison of Methods A, B, and C.1 based on green metrics.[42]

	3	4	5	6	7	8	9	10	11
Atom economy (AE)	**A:** 68.9 **B:** 77.0 **C.1:** 77.0	**A:** 67.3 **B:** 75.7 **C.1:** 75.7	**A:** 65.8 **B:** 74.4 **C.1:** 74.4	**A:** 63.2 **B:** 72.2 **C.1:** 72.2	**A:** 65.0 **B:** 73.7 **C.1:** 73.7	**A:** 69.6 **B:** 77.6 **C.1:** 77.6	**A:** 68.6 **B:** 76.7 **C.1:** 76.7	**A:** 65.8 **B:** 74.4 **C.1:** 74.4	**A:** 71.2 **B:** 78.9 **C.1:** 78.9
Real atom economy (RAE)	**A:** 0.084 **B:** – **C.1:** 0.580	**A:** 0.090 **B:** 0.0004 **C.1:** 0.390	**A:** 0.127 **B:** 0.0015 **C.1:** 0.488	**A:** 0.081 **B:** 0.011 **C.1:** 0.482	**A:** 0.128 **B:** 0.006 **C.1:** 0.197	**A:** 0.151 **B:** 0.025 **C.1:** 0.488	**A:** 0.120 **B:** 0.020 **C.1:** 0.468	**A:** 0.068 **B:** 0.029 **C.1:** 0.086	**A:** 0.055 **B:** 0.010 **C.1:** 0.417
Process mass intensity (PMI)	**A:** 11.96 **B:** – **C.1:** 1.73	**A:** 11.09 **B:** 2628.13 **C.1:** 2.56	**A:** 7.88 **B:** 659.59 **C.1:** 2.05	**A:** 12.39 **B:** 94.50 **C.1:** 2.07	**A:** 7.80 **B:** 167.38 **C.1:** 5.07	**A:** 6.63 **B:** 40.87 **C.1:** 2.04	**A:** 8.31 **B:** 49.92 **C.1:** 2.14	**A:** 14.72 **B:** 341.22 **C.1:** 11.61	**A:** 18.08 **B:** 98.11 **C.1:** 2.40

View Article Online
DOI: 10.1039/D6MR00048G

ARTICLE

Conclusions

In conclusion, this study introduces a ball-milling-based strategy as an efficient, scalable alternative to conventional solution-phase methods for the synthesis of carbonate compounds. The methodology eliminates the need for toxic solvents and organic bases while providing synthetically useful and operationally simple conditions. Importantly, the scalability of the process was successfully demonstrated on gram scale through the synthesis of Liffarome **II** and compound **9**, which were obtained in 42% and 74% yields, respectively, highlighting the practical applicability of the method beyond small-scale screening. Beyond the synthetic chemistry perspective, the approach enables direct access to structurally diverse carbonate-based aroma compounds, whose olfactory properties were systematically evaluated by an expert panel. The resulting fragrance profiles span multiple odor families, including floral, fruity, spicy, green, and gourmand notes, demonstrating clear relevance to fragrance science. Green metric analysis further supports the sustainability advantages of the mechanochemical approach. Compared to conventional solution-based methods, ball milling affords comparable or improved yields (up to 84%) while significantly reducing process waste and resource consumption. In particular, process mass intensity (PMI) values were reduced to as low as 1.73 for ball milling, compared to 11.96 for the traditional approach. Atom economy values were also higher for ball milling (72.2–78.9%) compared to the conventional method (63.2–71.2%), while real atom economy was substantially improved, reaching up to 0.580 for ball milling versus 0.151 for conventional methods. Taken together, these findings demonstrate that ball milling provides a practical, scalable, and sustainable platform for the synthesis of fragrance-related carbonate compounds, while also enabling access to structurally diverse molecules with unique olfactory properties. This combined chemical, green, and sensory relevance broadens the impact of the study for both synthetic chemistry and fragrance science communities.

Experimental

Materials and methods.

The commercially available reagents and solvent used in the reactions used as reagent grade and purchased from Sigma Aldrich, Fluka and Merck. They are used without any further purification. Solvents used in the extraction, flash column chromotography and TLC processes were distilled. Isobutyl chloroformate is an acutely toxic (H330) and volatile reagent with hazardous vapors (LC_{50} (inhalation) = 1.81 mg/L). Accordingly, all manipulations were performed in a well-ventilated fume hood. Aluminum sheets coated with 0.2 mm silica gel 60 F_{254} (Merck) are used in the analytical thin layer chromotography and displayed under UV light at 254 nm. Alcoholic phosphomolybdic acid solution at 50% is used to display some weekly conjugated molecules. Vacuum evaporation performed at 25–40 °C. Reported yields refers pure compounds that are dried under high vacuum. Nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$ on a Bruker Avance III Ultrashield 400 MHz NMR spectrometer. Using the remaining solvent signals as an internal reference ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm), chemical shifts δ are given in ppm downfield from tetramethylsilane (TMS). The resonance multiplicity for ^{1}H NMR is defined as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), and m (multiplet). Coupling constants J are stated in Hz. All spectrum recorded at 298K. Mechanochemical reactions were performed using a mixer mill (Retsch MM400) equipped with 25 mL polytetrafluoroethylene (PTFE) jars and 15 mm round PTFE milling balls. Milling was performed at a frequency of 30 Hz for 15, 30, or 60 min using a single ball per experiment. Thermo Scientific Nicolet iS10 ATR-IR spectrometer is used to record Infrared (IR) spectra. Signal locations are reported as wavenumbers (cm^{-1}). The intensities of IR band described as s (strong), m (medium), w (weak), br. (broad). The MS-service of METU Central Laboratory, Turkey, performed high-resolution mass spectrometry (HR-MS) analyses. Using a Time-of-Flight mass analyzer, spectra were analyzed in both positive or negative electrospray ionization modes. Masses are reported in m/z units as the molecule ion as $[M + Na]^+$.

Synthetic procedures

Method A. A 50 mL round-bottom flask was charged with the corresponding alcohol (1 equiv.) and DCM (5 mL per 1 g of alcohol), then the solution was cooled to 0 °C. Pyridine (1.3 equiv.) and alkyl chloroformate (1.2 equiv.) were added sequentially. The mixture was stirred at room temperature for 60 minutes. Following the reaction, DCM and excess pyridine were removed under vacuum. The desired products were isolated through column chromatography.

Method B. A 50 mL round-bottom flask was charged with the corresponding alcohol (1 equiv.) and 5 mL of distilled water, then the solution was cooled to 0 ˚C. NaOH (1.3 equiv.) and alkyl chloroformate (1.2 equiv.) were added sequentially. The mixture was stirred at room temperature for 60 minutes. Subsequently, the reaction mixture was extracted three times with 50 mL of EtOAc. The

combined organic layers were evaporated under vacuum, and the desired products were purified via column chromatography.

Method C.1, C.2, C.3. A 25 mL Teflon jar was charged with the corresponding alcohol (1 equiv.), NaOH (1.3 equiv.), and alkyl chloroformate (1.2 equiv.). When required, auxiliary agents such as neutral Al_2O_3 (3.0 g, Method C.2) or NaCl (1.5 g, Method C.3) were added. A Teflon ball was placed in the jar, and the mixture was shaken at 30 Hz for 30–60 minutes at room temperature. Following the reaction, the mixture was extracted three times with 50 mL of EtOAc. The combined organic layers were concentrated under vacuum, and the desired products were purified via column chromatography.

Compound 3: Method A: dec-9-en-1-ol (4.00 g, 25.60 mmol, 1 equiv), isobutyl chloroformate (4.20 g, 30.72 mmol, 1.2 equiv), pyridine (2.63 g, 33.28 mmol, 1.3 equiv.); yield: 3.13 g; 48%; **Method B:** dec-9-en-1-ol (100 mg, 0.64 mmol, 1 equiv), isobutyl chloroformate (105 mg, 0.77 mmol, 1.2 equiv), NaOH (33 mg, 0.83 mmol, 1.3 equiv.); yield: no reaction; **Method C.1:** ball milling (60 min, 30 Hz), dec-9-en-1-ol (100 mg, 0.64 mmol, 1 equiv), isobutyl chloroformate (105 mg, 0.77 mmol, 1.2 equiv), NaOH (33 mg, 0.83 mmol, 1.3 equiv.); yield: 138 mg; 84%; **Method C.2:** ball milling (30 min, 30 Hz), dec-9-en-1-ol (100 mg, 0.64 mmol, 1 equiv), isobutyl chloroformate (105 mg, 0.77 mmol, 1.2 equiv), NaOH (33 mg, 0.83 mmol, 1.3 equiv.), Al_2O_3 (neutral, 3.0 g); yield: 36 mg; 22%; **Method C.3:** ball milling (30 min, 30 Hz), dec-9-en-1-ol (100 mg, 0.64 mmol, 1 equiv), isobutyl chloroformate (105 mg, 0.77 mmol, 1.2 equiv), NaOH (33 mg, 0.83 mmol, 1.3 equiv.), NaCl (1.5 g); yield: 128 mg; 78%; colorless liquid; R_f = 0.66 (SiO_2; 12:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K); δ = 5.80 (ddt, J = 17.1, 10.2, 6.7 Hz, 1H), 4.99 (dd, J = 17.1, 1.5 Hz, 1H), 4.92 (dd, J = 10.2, 1.5 Hz, 1H), 4.12 (t, J = 6.7 Hz, 2H), 3.91 (d, J = 6.7 Hz, 2H), 2.07 – 1.91 (m, 3H), 1.71 – 1.62 (m, 2H), 1.37 – 1.27 (m, 10H), 0.95 ppm (d, J = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298K); δ = 155.6, 139.3, 114.3, 74.1, 68.2, 33.9, 29.5, 29.3, 29.2, 29.0, 28.8, 27.9, 25.8, 19.1 ppm; IR (ATR): $\tilde{\nu}$ = 2926 (m), 2856 (m), 1744 (s) cm^{-1}; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd. for $C_{15}H_{28}O_3Na^+$ 279.1936; Found 279.1951.

Compound 4: Method A: anisyl alcohol (5.00 g, 36.19 mmol, 1 equiv), isobutyl chloroformate (5.93 g, 43.43 mmol, 1.2 equiv), pyridine (3.72 g, 47.05 mmol, 1.3 equiv.); yield: 4.32 g; 50%; **Method B:** anisyl alcohol (100 mg, 0.72 mmol, 1 equiv), isobutyl chloroformate (119 mg, 0.87 mmol, 1.2 equiv), NaOH (38 mg, 0.94 mmol, 1.3 equiv.); yield: 2 mg; 1%; **Method C.1:** ball milling (60 min, 30 Hz), anisyl alcohol (100 mg, 0.72 mmol, 1 equiv), isobutyl chloroformate (119 mg, 0.87 mmol, 1.2 equiv), NaOH (38 mg, 0.94 mmol, 1.3 equiv.); yield: 100 mg; 58%; **Method C.2:** ball milling (30 min, 30 Hz), anisyl alcohol (100 mg, 0.72 mmol, 1 equiv), isobutyl chloroformate (119 mg, 0.87 mmol, 1.2 equiv), NaOH (38 mg, 0.94 mmol, 1.3 equiv.), Al_2O_3 (neutral, 3.0 g); yield: 7 mg; 4%; **Method C.3:** ball milling (30 min, 30 Hz), anisyl alcohol (100 mg, 0.72 mmol, 1 equiv), isobutyl chloroformate (119 mg, 0.87 mmol, 1.2 equiv), NaOH (38 mg, 0.94 mmol, 1.3 equiv.), NaCl (1.5 g); yield: 105 mg; 61%; colorless liquid; R_f = 0.52 (SiO_2; 4:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K); δ = 7.33 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 5.09 (s, 2H), 3.91 (d, J = 6.7 Hz, 2H), 3.81 (s, 3H), 2.02 – 1.90 (m, 1H), 0.93 ppm (d, J = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298K); δ = 160.0, 155.5, 130.5, 127.6, 114.1, 74.3, 69.5, 55.4, 27.9, 19.1 ppm; IR (ATR): $\tilde{\nu}$ = 2961 (m), 1740 (s) cm^{-1}; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd. for $C_{13}H_{18}O_4Na^+$ 261.1103; Found 261.1108.

Compound 5: Method A: phenethyl alcohol (3.50 g, 25.63 mmol, 1 equiv), isobutyl chloroformate (3.76 g, 30.75 mmol, 1.2 equiv), pyridine (2.64 g, 33.31 mmol, 1.3 equiv.); yield: 4.21 g; 74%; **Method B:** phenethyl alcohol (100 mg, 0.82 mmol, 1 equiv), isobutyl chloroformate (134 mg, 0.98 mmol, 1.2 equiv), NaOH (43 mg, 1.06 mmol, 1.3 equiv.); yield: 8 mg; 4%; **Method C.1:** ball milling (60 min, 30 Hz), phenethyl alcohol (100 mg, 0.82 mmol, 1 equiv), isobutyl chloroformate (134 mg, 0.98 mmol, 1.2 equiv), NaOH (43 mg, 1.06 mmol, 1.3 equiv.); yield: 135 mg; 74%; **Method C.2:** ball milling (30 min, 30 Hz), phenethyl alcohol (100 mg, 0.82 mmol, 1 equiv), isobutyl chloroformate (134 mg, 0.98 mmol, 1.2 equiv), NaOH (43 mg, 1.06 mmol, 1.3 equiv.), Al_2O_3 (neutral, 3.0 g); yield: 7 mg; 4%; **Method C.3:** ball milling (30 min, 30 Hz), phenethyl alcohol (100 mg, 0.82 mmol, 1 equiv), isobutyl chloroformate (134 mg, 0.98 mmol, 1.2 equiv), NaOH (43 mg, 1.06 mmol, 1.3 equiv.), NaCl (1.5 g); yield: 100 mg; 55%; colorless liquid; R_f = 0.80 (SiO_2; 4:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K); δ = 7.34 – 7.29 (m, 2H), 7.27 – 7.22 (m, 3H), 4.34 (t, J = 7.3 Hz, 2H), 3.91 (d, J = 6.7 Hz, 2H), 2.99 (t, J = 7.3 Hz, 2H), 2.03 – 1.91 (m, 1H), 0.95 ppm (d, J = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298K); δ = 155.4, 137.4, 129.1, 128.7, 126.8, 74.2, 68.3, 35.3, 27.9, 19.0 ppm; IR (ATR): $\tilde{\nu}$ = 2962 (m), 1741 (s) cm^{-1}; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd. for $C_{13}H_{18}O_3Na^+$ 245.1154; Found 245.1158.

Compound 6: Method A: furfuryl alcohol (3.00 g, 30.58 mmol, 1 equiv), isobutyl chloroformate (5.01 g, 36.70 mmol, 1.2 equiv), pyridine (3.14 g, 39.76 mmol, 1.3 equiv.); yield: 2.51 g; 41%; **Method B:** furfuryl alcohol (100 mg, 1.02 mmol, 1 equiv), isobutyl chloroformate (167 mg, 1.22 mmol, 1.2 equiv), NaOH (53 mg, 1.33 mmol, 1.3 equiv.); yield: 56 mg; 28%; **Method C.1:** ball milling (60 min, 30 Hz), furfuryl alcohol (100 mg, 1.02 mmol, 1 equiv), isobutyl chloroformate (167 mg, 1.22 mmol, 1.2 equiv), NaOH (53 mg, 1.33 mmol, 1.3 equiv.); yield: 154 mg; 76%; **Method C.2:** ball milling (30 min, 30 Hz), furfuryl alcohol (100 mg, 1.02 mmol, 1 equiv), isobutyl chloroformate (167 mg, 1.22 mmol, 1.2 equiv), NaOH (53 mg, 1.33 mmol, 1.3 equiv.), Al_2O_3 (neutral, 3.0 g); yield: 32 mg; 16%; **Method C.3:** ball milling (30 min, 30 Hz), furfuryl alcohol (100 mg, 1.02 mmol, 1 equiv), isobutyl chloroformate (167 mg, 1.22 mmol, 1.2 equiv), NaOH (53 mg, 1.33 mmol, 1.3 equiv.), NaCl (1.5 g); yield: 143 mg; 71%; colorless liquid; R_f = 0.69 (SiO_2; 6:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K); δ = 7.43 (dd, J = 1.9, 0.8 Hz, 1H), 6.45 (d, J = 3.2 Hz, 1H), 6.36 (dd, J = 3.2, 1.9 Hz, 1H), 5.10 (s, 2H), 3.93 (d, J = 6.7 Hz, 2H), 2.02 – 1.90 (m, 1H), 0.93 ppm (d, J = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298K); δ = 155.2, 149.0, 143.6, 111.3, 110.7, 74.4, 61.2, 27.9, 19.0 ppm; IR (ATR): $\tilde{\nu}$ = 2964 (m), 2877 (w), 1743 (s) cm^{-1}; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd. for $C_{10}H_{14}O_4Na^+$ 221.0790; Found 221.0795.

Compound 7: Method A: cycloheptanol (4.00 g, 35.03 mmol, 1 equiv), isobutyl chloroformate (5.74 g, 42.04 mmol, 1.2 equiv), pyridine (3.60 g, 45.54 mmol, 1.3 equiv.); yield: 5.12 g; 68%; **Method B:** cycloheptanol (100 mg, 0.88 mmol, 1 equiv), isobutyl

chloroformate (144 mg, 1.05 mmol, 1.2 equiv), NaOH (46 mg, 1.14 mmol, 1.3 equiv.); yield: 32 mg; 17%; **Method C.1:** ball milling (60 min, 30 Hz), cycloheptanol (100 mg, 0.88 mmol, 1 equiv), isobutyl chloroformate (144 mg, 1.05 mmol, 1.2 equiv), NaOH (46 mg, 1.14 mmol, 1.3 equiv.); yield: 57 mg; 30%; **Method C.2:** ball milling (30 min, 30 Hz), cycloheptanol (100 mg, 0.88 mmol, 1 equiv), isobutyl chloroformate (144 mg, 1.05 mmol, 1.2 equiv), NaOH (46 mg, 1.14 mmol, 1.3 equiv.), Al_2O_3 (neutral, 3.0 g); yield: 18 mg; 10%; **Method C.3:** ball milling (30 min, 30 Hz), cycloheptanol (100 mg, 0.88 mmol, 1 equiv), isobutyl chloroformate (144 mg, 1.05 mmol, 1.2 equiv), NaOH (46 mg, 1.14 mmol, 1.3 equiv.), NaCl (1.5 g); yield: 45 mg; 24%; colorless liquid; R_f = 0.59 (SiO_2; 12:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K); δ = 4.81 – 4.72 (m, 1H), 3.89 (d, J = 6.8 Hz, 2H), 2.02 – 1.92 (m, 3H), 1.75 – 1.64 (m, 4H), 1.57 – 1.53 (m, 4H), 1.49 – 1.38 (m, 2H), 0.94 ppm (d, J = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298K); δ = 155.1, 79.4, 73.9, 33.9, 28.4, 27.9, 22.8, 19.1 ppm; IR (ATR): $\tilde{\nu}$ = 2931 (m), 2863 (w), 1735 (s) cm^{-1}; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd. for $C_{12}H_{22}O_3Na^+$ 237.1467; Found 237.1471.

Compound 8: Method A: eugenol (5.00 g, 30.45 mmol, 1 equiv), isobutyl chloroformate (4.99 g, 36.54 mmol, 1.2 equiv), pyridine (3.13 g, 39.59 mmol, 1.3 equiv.); yield: 6.99 g; 87%; **Method B:** eugenol (100 mg, 0.61 mmol, 1 equiv), isobutyl chloroformate (100 mg, 0.73 mmol, 1.2 equiv), NaOH (32 mg, 0.79 mmol, 1.3 equiv.); yield: 128 mg; 80%; **Method C.1:** ball milling (60 min, 30 Hz), eugenol (100 mg, 0.61 mmol, 1 equiv), isobutyl chloroformate (100 mg, 0.73 mmol, 1.2 equiv), NaOH (32 mg, 0.79 mmol, 1.3 equiv.); yield: 113 mg; 70%; **Method C.2:** ball milling (30 min, 30 Hz), eugenol (100 mg, 0.61 mmol, 1 equiv), isobutyl chloroformate (100 mg, 0.73 mmol, 1.2 equiv), NaOH (32 mg, 0.79 mmol, 1.3 equiv.), Al_2O_3 (neutral, 3.0 g); yield: 50 mg; 31%; **Method C.3:** ball milling (30 min, 30 Hz), eugenol (100 mg, 0.61 mmol, 1 equiv), isobutyl chloroformate (100 mg, 0.73 mmol, 1.2 equiv), NaOH (32 mg, 0.79 mmol, 1.3 equiv.), NaCl (1.5 g); yield: 125 mg; 78%; colorless solid; R_f = 0.71 (SiO_2; 4:1 hexanes/ethyl acetate); m.p. = 29 – 31 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K); δ = 7.04 (d, J = 8.0 Hz, 1H), 6.80 – 6.74 (m, 2H), 5.95 (ddt, J = 16.9, 10.1, 6.7 Hz, 1H), 5.14 – 5.07 (m, 2H), 4.03 (d, J = 6.7 Hz, 2H), 3.83 (s, 3H), 3.38 (d, J = 6.7 Hz, 2H), 2.11 – 1.99 (m, 1H), 0.99 ppm (d, J = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298K); δ = 153.7, 151.1, 139.3, 138.6, 137.1, 122.2, 120.7, 116.3, 112.9, 74.9, 55.9, 40.2, 27.9, 19.0 ppm; IR (ATR): $\tilde{\nu}$ = 2967 (m), 2936 (w), 2877 (w), 1754 (s) cm^{-1}; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd. for $C_{15}H_{20}O_4Na^+$ 287.1259; Found 287.1259.

Compound 9: Method A: vanillin (4.50 g, 29.58 mmol, 1 equiv), isobutyl chloroformate (4.85 g, 35.49 mmol, 1.2 equiv), pyridine (3.04 g, 38.45 mmol, 1.3 equiv.); yield: 5.09 g; 68%; **Method B:** vanillin (100 mg, 0.66 mmol, 1 equiv), isobutyl chloroformate (108 mg, 0.79 mmol, 1.2 equiv), NaOH (34 mg, 0.85 mmol, 1.3 equiv.); yield: 105 mg; 63%; **Method C.1:** ball milling (60 min, 30 Hz), vanillin (100 mg, 0.66 mmol, 1 equiv), isobutyl chloroformate (108 mg, 0.79 mmol, 1.2 equiv), NaOH (34 mg, 0.85 mmol, 1.3 equiv.); yield: 113 mg; 68%; **Method C.2:** ball milling (30 min, 30 Hz), vanillin (100 mg, 0.66 mmol, 1 equiv), isobutyl chloroformate (108 mg, 0.79 mmol, 1.2 equiv), NaOH (34 mg, 0.85 mmol, 1.3 equiv.), Al_2O_3 (neutral, 3.0 g); yield: 15 mg; 9%; **Method C.3:** ball milling (30 min, 30 Hz), vanillin (100 mg, 0.66 mmol, 1 equiv), isobutyl chloroformate (108 mg, 0.79 mmol, 1.2 equiv), NaOH (34 mg, 0.85 mmol, 1.3 equiv.), NaCl (1.5 g); yield: 106 mg; 64%; white solid; R_f = 0.41 (SiO_2; 4:1 hexanes/ethyl acetate); m.p. = 108 – 110 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K); δ = 9.95 (s, 1H), 7.52 – 7.46 (m, 2H), 7.32 (d, J = 7.9 Hz, 1H), 4.06 (d, J = 6.7 Hz, 2H), 3.92 (s, 3H), 2.12 – 2.00 (m, 1H), 1.00 ppm (d, J = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298K); δ = 191.1, 152.8, 152.2, 145.2, 135.4, 124.9, 123.1, 111.0, 75.4, 56.3, 28.0, 18.9 ppm; IR (ATR): $\tilde{\nu}$ = 2965 (m), 2913 (w), 1757 (s) cm^{-1}; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd. for $C_{13}H_{16}O_5Na^+$ 275.0895; Found 275.0926.

Compound 10: Method A: 2-pentanol (3.00 g, 34.03 mmol, 1 equiv), benzyl chloroformate (6.97 g, 40.84 mmol, 1.2 equiv), pyridine (3.50 g, 44.24 mmol, 1.3 equiv.); yield: 2.27 g; 30%; **Method B:** 2-pentanol (100 mg, 1.13 mmol, 1 equiv), benzyl chloroformate (232 mg, 1.36 mmol, 1.2 equiv), NaOH (59 mg, 1.47 mmol, 1.3 equiv.); yield: 16 mg; 6%; **Method C.1:** ball milling (60 min, 30 Hz), 2-pentanol (100 mg, 1.13 mmol, 1 equiv), benzyl chloroformate (232 mg, 1.36 mmol, 1.2 equiv), NaOH (59 mg, 1.47 mmol, 1.3 equiv.); yield: 34 mg; 13%; **Method C.2:** ball milling (30 min, 30 Hz), 2-pentanol (100 mg, 1.13 mmol, 1 equiv), benzyl chloroformate (232 mg, 1.36 mmol, 1.2 equiv), NaOH (59 mg, 1.47 mmol, 1.3 equiv.), Al_2O_3 (neutral, 3.0 g); yield: 15 mg; 6%; **Method C.3:** ball milling (30 min, 30 Hz), 2-pentanol (100 mg, 1.13 mmol, 1 equiv), benzyl chloroformate (232 mg, 1.36 mmol, 1.2 equiv), NaOH (59 mg, 1.47 mmol, 1.3 equiv.), NaCl (1.5 g); yield: 48 mg; 19%; colorless liquid; R_f = 0.64 (SiO_2; 9:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K); δ = 7.41 – 7.31 (m, 5H), 5.15 (s, 2H), 4.84 – 4.74 (m, 1H), 1.69 – 1.59 (m, 1H), 1.54 – 1.43 (m, 1H), 1.41 – 1.29 (m, 2H), 1.27 (d, J = 6.3 Hz, 3H), 0.91 ppm (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298K); δ = 155.0, 135.5, 128.7, 128.6, 128.4, 75.6, 69.4, 38.1, 20.0, 18.7, 14.0 ppm; IR (ATR): $\tilde{\nu}$ = 2960 (m), 2874 (w), 1736 (s) cm^{-1}; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd. for $C_{13}H_{18}O_3Na^+$ 245.1154; Found 245.1154.

Compound 11:

Method A: vanillin (4.00 g, 26.29 mmol, 1 equiv), benzyl chloroformate (5.38 g, 31.55 mmol, 1.2 equiv), pyridine (2.70 g, 34.18 mmol, 1.3 equiv.); yield: 2.14 g; 28%; **Method B:** vanillin (100 mg, 0.66 mmol, 1 equiv), benzyl chloroformate (135 mg, 0.79 mmol, 1.2 equiv), NaOH (34 mg, 0.85 mmol, 1.3 equiv.); yield: 54 mg; 29%; **Method C.1:** ball milling (60 min, 30 Hz), vanillin (100 mg, 0.66 mmol, 1 equiv), benzyl chloroformate (135 mg, 0.79 mmol, 1.2 equiv), NaOH (34 mg, 0.85 mmol, 1.3 equiv.); yield: 112 mg; 60%; **Method C.2:** ball milling (30 min, 30 Hz), vanillin (100 mg, 0.66 mmol, 1 equiv), benzyl chloroformate (135 mg, 0.79 mmol, 1.2 equiv), NaOH (34 mg, 0.85 mmol, 1.3 equiv.), Al_2O_3 (neutral, 3.0 g); yield: 17 mg; 9%; **Method C.3:** ball milling (30 min, 30 Hz), vanillin (100 mg, 0.66 mmol, 1 equiv), benzyl chloroformate (135 mg, 0.79 mmol, 1.2 equiv), NaOH (34 mg, 0.85 mmol, 1.3 equiv.), NaCl (1.5 g); yield: 41 mg; 22%; white solid; R_f = 0.63 (SiO_2; 2:1 hexanes/ethyl acetate); m.p. = 105 – 107 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K); δ = 9.94 (s, 1H), 7.51 – 7.48 (m, 2H), 7.47 – 7.36 (m, 5H), 7.32 (d, J = 8.0 Hz, 1H), 5.29 (s, 2H), 3.87 ppm (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298K); δ = 191.1, 152.6, 152.1, 145.1, 135.5, 134.8, 128.9, 128.8, 128.6, 124.8, 123.0, 111.1, 70.9, 56.2 ppm; IR (ATR): $\tilde{\nu}$ = 3013 (w),1757 (s) cm^{-1}; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd. for $C_{16}H_{14}O_5Na^+$ 309.0739; Found 309.0750.

Author contributions

C. B., M. E. Ç., and M. M. performed the experiments. This work was conceptualized by A. A., A. B., and C. D. The first draft of the manuscript was prepared by C. D. and the final version was edited and revised by A. A. and A. B. All the authors read and approved the final manuscript.

Conflicts of interest

There are no conflicts to declare.

Data availability

Supplementary information (SI): Copies of ^{1}H NMR, and $^{13}C\{^{1}H\}$ NMR spectra, HRMS data, and IR spectra.

Acknowledgements

C.D. acknowledges the financial support provided by the GEBIP Award of the Turkish Academy of Sciences. This study was supported by the Middle East Technical University Scientific Research Projects Coordination Unit (Project No: ADEP-103-2023-11269). We express our gratitude to MG International Fragrance Company and their panelists Jorge Lee, Edip Göktuğ Kumral, Koray Sevinç, Ceyhun Arman for their invaluable contribution to the determination of the olfactory characteristics of the new carbonate molecules.

Notes and references

1 R. Cayuela Valencia, The Future of the Chemical Industry by 2050, Wiley, Chichester, 2013.
2 M. Filonchyk, M. P. Peterson, H. Yan, A. Gusev, L. Zhang, Y. He and S. Yang, *Sci. Total Environ.* 2024, **944**, 173895. DOI: 10.1016/j.scitotenv.2024.173895
3 J. Huo, Z. Wang, C. Oberschelp, G. Guillén-Gosálbez and S. Hellweg, *Green Chem.* 2022, **25**, 415–430. DOI: 10.1039/D2GC03047K
4 P. Gabrielli, L. Rosa, M. Gazzani, R. Meys, A. Bardow, M. Mazzotti and G. Sansavini, *One Earth* 2023, **6**, 682–704. DOI: 10.1016/j.oneear.2023.05.006
5 J. A. Tickner, K. Geiser, S. Baima, *Environment* 2022, **64**, 22–36. DOI: 10.1080/00139157.2022.2021793
6 O. R. P. David and F. Doro, *Eur. J. Org. Chem.* 2023, **26**, e202300900. DOI: 10.1002/ejoc.202300900
7 S. Gutiérrez, S. Overmans, G. B. Wellman, V. G. Samaras, C. Oviedo, M. Gede, G. Szekely and K. J. Lauersen, *Green Chem.* 2023, **26**, 2577–2591. DOI: 10.1039/D3GC03708H
8 P. R. Tambe, G. D. Yadav, *J. Chem. Sci.* 2017, **129**, 1771–1779. DOI: 10.1007/s12039-017-1395-y
9 M. Kleoff, P. Kiler and P. Heretsch, *Beilstein J. Org. Chem.* 2022, **18**, 754–768. DOI: 10.3762/bjoc.18.76
10 J. D. Moseley and C. O. Kappe, *Green Chem.* 2011, **13**, 794–806. DOI: 10.1039/C0GC00823K
11 M. Worzakowska, *Molecules* 2015, **20**, 10594–10603. DOI: 10.3390/molecules200610594
12 A. Pawełczyk and L. Zaprutko, *Eur. J. Med. Chem.* 2006, **41**, 586–591. DOI: 10.1016/j.ejmech.2005.09.012
13 F. Elterlein, N. Bugdahn and P. Kraft, *Chem.–Eur. J.* 2024, **30**, e202400006. DOI: 10.1002/chem.202400006
14 P. Anastas and N. Eghbali, *Chem. Soc. Rev.* 2010, **39**, 301–312. DOI: 10.1039/B918763B
15 M. Wohlgemuth, S. Schmidt, M. Mayer, W. Pickhardt, S. Graetz and L. Borchardt, *Angew. Chem. Int. Ed.* 2024, **63**, e202405342. DOI: 10.1002/anie.202405342
16 A. H. Fattahi, M. G. Dekamin and J. H. Clark, *Sci. Rep.* 2023, **13**, 2803. DOI: 10.1038/s41598-023-29568-y
17 C. Xu, S. De, A. M. Balu, M. Ojeda and R. Luque, *Chem. Commun.* 2015, **51**, 6698–6713. DOI: 10.1039/C4CC09876E
18 I. Sović, S. Lukin, E. Meštrović, I. Halasz, A. Porcheddu, F. Delogu, P. C. Ricci, F. Caron, T. Perilli, A. Dogan and E. Colacino, *ACS Omega* 2020, **5**, 28663–28672. DOI: 10.1021/acsomega.0c03756
19 M. Pérez-Venegas, T. Arbeloa, J. Bañuelos, I. López-Arbeloa, N. E. Lozoya-Pérez, B. Franco, H. M. Mora-Montes, J. L. Belmonte-Vázquez, C. I. Bautista-Hernández, E. Peña-Cabrera and E. Juaristi, *Eur. J. Org. Chem.* 2021, **2021**, 253–265. DOI: 10.1002/ejoc.202001267
20 A. Krusenbaum, S. Grätz, G. T. Tigineh, L. Borchardt and J. G. Kim, *Chem. Soc. Rev.* 2022, **51**, 2873–2905. DOI: 10.1039/D1CS01093J
21 M. A. Rasool, P. P. Pescarmona and I. F. J. Vankelecom, *ACS Sustain. Chem. Eng.* 2019, **7**, 13774–13785. DOI: 10.1039/D3RA04735K
22 'The Good Scents Company, http://www.thegoodscentscompany.com/data/rw1059431.html, (accessed December 2010).
23 "'The Good Scents Company, http://www.thegoodscentscompany.com/data/rw1028731.html, (accessed December 2010).
24 "'The Good Scents Company, http://www.thegoodscentscompany.com/data/rw1019571.html, (accessed December 2010).
25 "'The Good Scents Company, http://www.thegoodscentscompany.com/data/rw1013531.html, (accessed December 2010).
26 "'The Good Scents Company, http://www.thegoodscentscompany.com/data/rw1027551.html, (accessed December 2010).
27 B. Schäffner, F. Schäffner, S. P. Verevkin and A. Börner, *Chem. Rev.* 2010, **110**, 4554–4581. DOI: 10.1021/cr900393d
28 A.-A. G. Shaikh and S. Sivaram, *Chem. Rev.* 1996, **96**, 951–976. DOI: 10.1021/cr950067i
29 W. S. Putro, S. Ijima, S. Matsumoto, S. Hamura, M. Yabushita, K. Tomishige and N. Fukaya, J. C. Choi, *RSC Sustain.* 2024, **2**, 1613–1620. DOI:10.1021/acssuschemeng.5c13182
30 I. J. Drake, K. L. Fujdala, A. T. Bell and T. D. Tilley, *J. Catal.* 2005, **230**, 14–27. DOI: 10.1002/anie.200462473
31 E. J. C. Lopes, A. P. C. Ribeiro and L. M. D. R. S. Martins, *Catalysts* 2020, **10**, 479. DOI: 10.3390/catal10050479
32 T. Hong, J. Guan, W. Zhou, S. Tan and Z. Cai, *Cell Rep. Phys. Sci.* 2025, **6**, 102785. DOI: 10.1016/j.xcrp.2025.102785
33 P. Tundo and F. Aricò, *ChemSusChem* 2023, **16**, e202300748. DOI: 10.1002/cssc.202300748
34 G. Leonardos, D. Kendall and N. Barnard, *J. Air Pollut. Control Assoc.* 1969, **19**, 91–95. DOI:10.1080/00022470.1969.10466465
35 S. Uema, N. Kojima and T. Yamada, *Chem. Lett.* 2024, **53**, upea001. DOI: 10.1093/chemle/upae001.
36 D. H. Dethe, S. Juyal, N. Sharma and U. Kundu, *Org. Lett.* 2024, **26**, 3010–3013. DOI: 10.1021/acs.orglett.4c00605
37 T. Schlatzer, H. Schröder, M. Trobe, C. Lembacher-Fadum, S. Stangl, C. Schlögl, H. Weber and R. Breinbauer, *Adv. Synth. Catal.* 2020, **362**, 331–336. DOI: 10.1002/adsc.201901250
38 J. L. Howard, Q. Cao and D. L. Browne, *Chem. Sci.* 2018, **9**, 3080–3094. DOI: 10.1039/C7SC05371A

39 T. Friščić, S. L. Childs, S. A. A. Rizvi, and W. Jones, CrystEngComm, 2009, **11**, 418–426. DOI: 10.1039/B815174A
40 C. Irawan, S. Indryati, E. S. Lestari and A. Hidaningrum, Supriyono, *Orient. J. Chem.* 2018, **34**, 394–400. DOI: 10.13005/ojc/360332
41 C. S. Cortez-Pereira, A. R. Baby, M. V. R. Velasco and *J. Cosmet. Dermatol.* 2010, **9**, 230–241. DOI: 10.1155/2012/204830
42 N. Fantozzi, J. N. Volle, A. Porcheddu, D. Virieux, F. García and E. Colacino, *Chem. Soc. Rev.* 2023, **52**, 6680–6714. DOI: 10.1039/D2CS00997H

View Article Online
DOI: 10.1039/D6MR00048G

Data availability

Supplementary information (SI): Copies of ^{1}H NMR, and $^{13}C\{^{1}H\}$ NMR spectra, HRMS data, and IR spectra.