Selective Removal of Chlorinated Impurities from (*R*)-Carvone Using an Industrial Alkaline Sulfite Process

Nicolae Florin Popa[1], Cosmina Andrea Chirilă[2], Daniela Camelia Sebeșan[2], Andrea Corina Bărbos[2], Sandra Florina Lele [1], Alexandra Iepan [1], Dumitru Popescu[1], Florica Emilia Morariu [1]

[1]*University of Life Sciences "King Mihai I" from Timisoara, Faculty of Bioengineering of Animal Resources, 300645, Calea Aradului No. 119, Timisoara, Romania*
[2]*Francesco Saverio Nitti Economic College, Strada Corbului, nr.7, 300239, Timisoara, Romania*

Abstract

Chlorinated impurities present in crude (*R*)-Carvone, ($C_{10}H_{14}O$), preferred IUPAC name 2-Methyl-5-(prop-1-en-2-yl) cyclohex-2-en-1-one, resulted in chemical synthesis, represent a significant challenge for its utilization, as they may compromise product stability, safety and applicability in food, fragrance and pharmaceutical formulations. This study presents an industrial validated process, for the selective removal of chlorinated compounds, using an alkaline sulfite system, under moderate reaction conditions. The method employs a biphasic mixture of sodium hydroxide (NaOH), sodium sulfite (Na_2SO_3), isopropanol (C_3H_8O) and controlled acetic acid ($C_2H_4O_2$) addition, in a stirred reactor, equipped with reflux and solvent recovery units, followed by solvent distillation and recycling steps. Process operates at temperatures between 60 and 90^0C and includes a closed loop recycling stage, which improves reagent utilization and reduces waste generation. The proposed approached enables efficient conversion and removal of chlorinated terpene impurities, while preserving the structural integrity of the targeted ketone. The integration of reaction and purification in a single industrial unit, combined with solvent recovery and neutralization stages, provides a scalable and economically attractive solution for the production of hi purity (*R*)-Carvone. This work demonstrates a practical and selective dichlorination strategy suitable for large scale terpene processing.

Keywords: carvone, dichlorination, impurities, ketones, limonene, terpene.

1. Introduction

(R)-Carvone is an optically active monoterpene ketone wildly used in the food, fragrance, cosmetic and pharmaceutical industries, due to its characteristic spearmint aroma and biological activity [1, 21]. As a natural occurring compound, it is present in high concentrations in spearmint oil, however the large-scale industrial demand is frequently met through the chemical transformation of abundant terpene feedstocks such as (*R*)-Limonene ($C_{10}H_{16}$) derived from citrus processing byproducts. The conversion of (*R*)-Limonene to (*R*)-Carvone represents an economically attractive route that enables the valorization of renewable raw materials such as citrus peel, while ensuring consistent product quality and supply [2, 9, 19].

Industrial synthesis of (*R*)-Carvone from (*R*)-Limonene typically involve sequential oxidation steps. In a common pathway, (*R*)-Limonene undergoes selective allylic oxidation to form (*R*)-Carveol, followed by further oxidation of the allylic alcohol to the corresponding ketone, (*R*)-Carvone. These transformations may be carried out using various catalytic systems, including metal-based

* Corresponding author: Nicolae Florin Popa, popa_ncl@yahoo.com; tel: +04 0722.688.459

oxidants, radical mediators or hypochlorite-based oxidation systems, depending on the specific configuration of the process and economic considerations [3, 19]. While such methods can provide satisfactory yields and scalability, the process will generate related impurities.

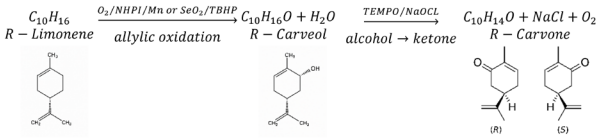

Figure.1 Conversion of (R)-Limonene to (R)-Carvone [4]

Catalytic system: O_2/NHPI-Co (II)/Mn (II), for allylic oxidation where: NHPI - N-hydroxy phthalimide (radical mediator), Co (II) salt - typically cobalt (II) acetate, Co $(OAc)_2$ Mn (II) salt - typically manganese (II) acetate, Mn $(OAc)_2$; or catalytic system SeO_2 / TBHP where: SeO_2 - selenium dioxide (allylic oxidation catalyst) TBHP - tert-butyl hydroperoxide (oxidant)

TEMPO catalyzed oxidation using sodium hypochlorite (NaOCl) where: TEMPO - 2,2,6,6-tetramethylpiperidin-1-oxyl (nitroxyl radical catalyst) NaOCl - sodium hypochlorite (oxidant)

In particular, oxidation systems involving chloride oxidation reagents or acidic neutralization steps generate chlorinated terpene byproducts. Under these conditions, reactive chlorine compounds may interact with unsaturated terpene skeleton through electrophilic addition or substitution reactions, leading to the formation of allylic chlorides or addition type derivates. Even when present in small trace amounts, such chlorinated impurities can adversely affect product stability, odor profile, regulatory compliance and other downstream applications, especially in food and pharmaceutical industries. Effective removal of this contaminants is an important step in the industrial production of high purity (*R*)-Carvone [5, 23].

Various purification approaches have been studied for terpene systems, including distillation, adsorption and chemical treatment, however physical separations alone may not always be sufficient, when impurity's possess similar volatility and polarity as the targeted compound. In such cases, selective chemical conversion of the undesired species, into more easily separable forms represent a practical and scalable strategy [6].

The present work describes an industrially implemented process for selective removal of chlorinated terpene impurities from crude (*R*)-Carvone using an alkaline sulfite system. The method is based on the treatment of crude terpene mixture with sodium hydroxide and sodium sulfite in an isopropanol water medium, followed by controlled acid addition, solvent distillation and recycling steps, within a single reactor unit [7].

The objective of this study is to present the operational concept and effectiveness of this alkaline sulfite assisted dichlorination strategy highlighting its suitability for large scale production of high purity *(R)*-Carvone from Limonene derived intermediates [8, 19].

2. Materials and methods

Alkaline Sulfite Treatment Procedure (Stage 1)

The dichlorination process is carried out in a 2000L stirred reactor, equipped with mechanical agitation, a reflux condenser, temperature and pressure control, and a vacuum feed system [9, 18].

A 30% (w/w) aqueous sodium hydroxide solution (NaOH) is prepared in a separate vessel. Isopropanol (C_3H_8O) is introduced into the reactor, followed by the addition of sodium sulfite (Na_2SO_3) under continuous stirring at low temperature. After charging, the reactor is closed and the mixture is gradually heated to 40-50^{0}C to ensure complete homogenization [10, 20].

Crude (*R*)-carvone is introduced into the reactor and the reaction mixture is subsequently heated to 80^{0}C, after which acetic acid (CH_3COOH) is added dropwise from the top inlet over a period of approximately 1.5 hours, under continuous agitation. Upon completion acid addition, the reactor is sealed and the temperature is increased to 90^{0}C. During this stage, the reactor is intermittently vented to release accumulated gases. The reaction mixture is maintained under these conditions for approximately 5 hours to ensure treatment completion. After completion, water is introduced into the reactor, and the system is gradually opened to initiate distillation of the isopropanol water mixture. The amount of separated organic phase (oil) is monitored continuously [11, 19].

In cases where phase separation is insufficient in the receiving vessel, additional 30% sodium hydroxide solution is introduced until approximately 2-3kg of oil is recovered, followed by the addition of the remaining sodium hydroxide solution to complete the treatment process. After phase separation, the aqueous layer is removed from the decantation vessel, and the distillation process is continued until completion [12, 24].

Secondary Alkaline Sulfite Treatment and Recycling Process (Stage 2)

Following completion of Stage 1 and separation of the aqueous phase, the remaining concentrated reaction mixture is subjected to a recycling treatment in order to improve impurity removal efficiency and overall process yield. The concentrated solution obtained from the previous stage is reintroduced into the reactor, with isopropanol (C_3H_8O) under continuous stirring. The reaction mixture is heated again at 60-70^{0}C to ensure adequate homogenization prior to further treatment [13].

Acetic acid (CH_3COOH) is subsequently added again in a controlled manner under reflux conditions over a period of approximately 1.5 hours. After completion of the addition, the temperature is increased to 90^{0}C, and the system is maintained at a pressure of approximately 0.6 bar. The mixture is stirred and refluxed under these conditions for an additional 4 hours to allow further conversion and removal of residual chlorinated impurities. During this stage, the reactor is intermittently vented to release accumulated gases and maintain stable operating conditions [14, 23].

Upon completion of the reaction period, water is introduced into the reactor, and distillation of the isopropanol water mixture is initiated. The distillate is collected into aqueous fractions (B1, B2, B3), corresponding to approximately 190kg, 160kg, and 120kg [15].

Phase separation is monitored using a Florentine receiver. In cases where the organic phase did not separate efficiently, additional 30% (w/w) sodium hydroxide solution is introduced, incrementally to promote phase disengagement and facilitate recovery of the organic fraction, until approximately 1.5 kg of oil is recovered [16].

After sufficient phase separation is achieved, the remaining sodium hydroxide solution is added, and the distillation process is continued, with transfer through the Florentine separator until completion. The organic phase containing purified (*R*)-carvone is collected, while the aqueous phase is removed [17, 21, 24].

Neutralization (Stage 3)

Following completion of the distillation process, the residual solution in the reactor is treated with 30% hydrogen peroxide (H_2O_2) and 35% acetic acid under controlled conditions. This neutralization step ensures the oxidation of remaining reducing agents and the adjustment of the pH to near-neutral values, thereby improving the stability and handling in this final process stream [18, 19].

Following completion of this stage, a mandatory sample is collected to verify the effective removal of chlorinated compounds. In cases where the desired dichlorination is achieved but residual impurities remain due to external contamination, an additional distillation step is applied to further purify the product. [19].

3. Results and discussion

All batches proceeded under relatively similar operating conditions, demonstrating excellent reproducibility of the process. Material losses were maintained within a narrow range of approximately 0.05-0.2% per batch, with the majority of these losses attributed to minor operational and handling errors rather than inherent process limitations. Over the entire series of batches, the cumulative loss of (*R*)-carvone amounted to approximately 16.9kg, which remains acceptable for an industrial-scale operation of this type. The process exhibited stable performance in terms of product quality, with the final purity of (*R*)-carvone consistently ranging between 98.0% and 99.2%. These results indicate that the alkaline sulfite treatment, combined with the recycling stages, provides a reliable and efficient approach for the purification of (*R*)-carvone, ensuring both high product quality and controlled material losses across multiple production cycles [20, 21, 22].

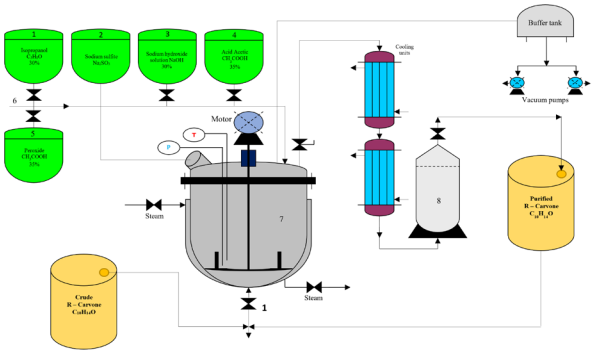

Figure 2. Industrial continuous installation for eliminating Cl form (*R*)-Carvone [Original]
1. Isopropanol tank, 2. Sodium sulfite tank, 3. Sodium hydroxide tank, 4. acetic acid tank, 5. Peroxide tank, 6. water inlet, 7. reaction vessel, 8. Florentine flask

The determination of chlorine content was performed using complementary analytical techniques. Total chlorine was quantified by combustion microcoulometry using a Mitsubishi AQF-2100H analyzer. Chloride ions in the aqueous phase were measured by ion chromatography employing a Thermo Scientific Dionex ICS-3000 system. In addition, gas chromatography was used to monitor residual organic impurities and confirm product purity, using an Agilent 7890A GC instrument [23, 24]

Table 1. Table 1. Elimination Cl form (*R*)-Carvone

Batch No	Crude (R)-carvone (kg)	Initial Cl (ppm)	Final Cl (ppm)	Cl removal (%)	Final purity (%)	(R)-carvone Final (kg)
1	800	1278	23	98.2	98.6	799.5
2	800	1342	32	97.6	98.8	798.9
3	800	1450	31	97.9	98	799
4	800	1258	29	97.7	98.1	797.9
5	800	1354	30	97.8	98.2	798.6
6	800	1284	28	97.8	98.4	799.6
7	800	1489	36	97.6	98.4	798.7
8	800	1254	24	98.1	98.1	795.6
9	800	1365	32	97.7	99.2	799.4
10	800	1701	24	98.6	98.6	798.6
11	800	1389	28	98.0	98.6	799.2
12	800	1462	31	97.9	98.4	798.1
TOTAL	9600					9583.1

As we can see by the data presented in Table 1 and Figure 3, the most favorable overall performance was observed in batch 6. Although the efficiency of chlorine removal in this case was slightly lower compared to other batches, such as batch 10, the associated overall material losses were significantly reduced, while the residual chlorine content remained within the acceptable regulatory limits. In contrast, the least satisfactory results were obtained in batch 8, where higher quantitative losses were recorded, most likely due to operational deviations errors, human errors, measurement, calibration and machine malfunctioning.

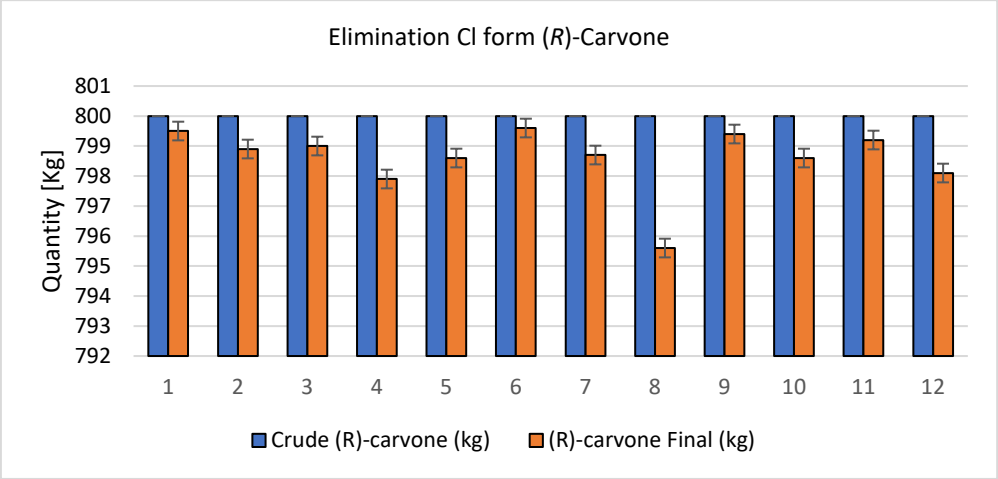

Figure 3. Elimination Cl form (*R*)-Carvone final results

The highest chlorine removal efficiency was achieved in batch 10, with approximately 98.6% of the initial chlorine content eliminated, whereas the lowest efficiencies were observed for batches 2 and 7, where chlorine removal reached approximately 97.7%. Despite these variations, all batches were within the specified chlorine limits, and no additional distillation was required to address external contamination. Overall, the process demonstrated consistent performance, yielding a stable and economically efficient purification strategy.

4. Conclusions

The initial combination of isopropanol and sodium sulfite under stirring at 40-50^{0}C establishes a homogeneous solvent environment that facilitates the dissolution and dispersion of sulfite ions. Isopropanol acts as a polar organic medium, improving mass transfer between phases and promoting effective solvation of the inorganic salt. At this stage, sodium sulfite dissociates into reactive sulfite compounds, which are subsequently available for interaction with chlorine containing compounds introduced in later stages.

$$Na_2SO_3(s) \rightarrow 2Na^+(aq) + SO_3^{2-}(aq)$$

$$SO_3^{2-} + H_2O \leftrightarrow HSO_3^- + OH^-$$

$$HSO_3^- + H^+ \leftrightarrow SO_2(aq) + H_2O$$

After adding (*R*)-carvone and starting controlled acidification it shifts the sulfite equilibrium, generating a reactive mixture of sulfite (SO_3^{2-}) and bisulfite (HSO_3^-), which enhances interaction with chlorine containing compounds. Bisulfite is particularly effective in reacting with electrophilic chlorine intermediates and promotes their conversion into stable chloride ions. Simultaneously, the hi temperature improves reaction kinetics and mass transfer between phases.

$$SO_3^{2-} + H^+ \leftrightarrow HSO_3^-$$

$$HSO_3^- + HOCl \rightarrow SO_4^{2-} + Cl^- + H^+$$

The system is given time and temperature to drive the earlier equilibria toward completion. Residual reactive chlorine compounds are further consumed by sulfite/bisulfite, while partially transformed organochlorine impurities continue to react and become more polar or less reactive. The elevated temperature also improves phase contact and accelerates the conversion of unstable intermediates, thereby promoting chemical stabilization before the separation step.

The additional sodium hydroxide introduced at this stage primarily promotes phase disengagement rather than initiating a new reaction pathway. By increasing alkalinity, residual acetic acid is converted into water soluble acetate compounds, while bisulfite is shifted back toward sulfite, thereby stabilizing the aqueous phase and reducing emulsion persistence. As a result, ionic chlorine containing compounds and other polar impurities are preferentially retained in the aqueous layer, enabling more efficient recovery of the organic phase enriched in (*R*)-carvone.

$$CH_3COOH + OH^- \rightarrow CH_3COO^- + H_2O$$

$$HSO_3^- + OH^- \rightarrow SO_3^{2-} + H_2O$$

Following completion of Stage 1, the residual reaction mixture is reconditioned by the re-addition of isopropanol and reheating to 60-70^{0}C under continuous stirring. This step restores homogeneity and facilitates redistribution of sulfite compounds within the system. Under these conditions, the sulfite bisulfite equilibrium is reestablished, ensuring that reactive sulfur compounds remain available for further interaction with residual chlorine containing impurities in the subsequent treatment stage.

During the secondary treatment stage, controlled addition of acetic acid under reflux conditions re-establishes a reactive sulfite bisulfite equilibrium, enhancing the system's ability to interact with residual chlorine containing compounds. Elevated temperature and extended reaction time promote further reduction of reactive chlorine intermediates and facilitate the transformation of persistent organochlorine impurities into more polar derivatives. Intermittent venting ensures removal of accumulated volatile compounds and maintains stable reaction conditions throughout the process.

$$R - Cl + SO_3^{2-} \rightarrow R - SO_3^- + Cl^-$$

Upon completion, water addition promotes phase separation by increasing the polarity contrast between the organic and aqueous phases, facilitating transfer of ionic and polar compounds into the aqueous layer. Subsequent distillation of the isopropanol water mixture enhances separation efficiency by reducing solvent content and minimizing mutual solubility. Incremental addition of sodium hydroxide, when required, improves phase disengagement through neutralization of residual acidic components and suppression of emulsion formation. The organic phase enriched in (R)-carvone is thereby effectively separated from the aqueous phase containing inorganic salts and polar impurities.

Following completion of the distillation process, the residual solution is subjected to oxidative neutralization using hydrogen peroxide and acetic acid. Hydrogen peroxide converts residual sulfite and bisulfite compounds into stable sulfate ions, thereby eliminating remaining reducing agents from the system. Concurrently, acetic acid adjusts the pH to near neutral values, through controlled neutralization of excess alkalinity. This combined treatment ensures chemical stabilization of the process streams and improves their handling, storage, and environmental compatibility.

$$SO_3^{2-} + H_2O_2 \rightarrow SO_4^{2-} + H_2O$$

$$HSO_3^- + H_2O_2 \rightarrow SO_4^{2-} + H_2O + H^+$$

$$OH^- + CH_3COOH \rightarrow +CH_3COO^- + H_2O$$

Chlorine present in crude (R)-carvone, either as reactive chlorine compounds or as organochlorine impurities, is eliminated through a combined chemical and physical process. Initially, sulfite ions (SO_3^{2-}) reduce reactive chlorine compounds such as hypochlorous acid (HOCl) and chlorine (Cl_2) to stable chloride ions (Cl^-). Concurrently, chlorinated organic compounds are transformed into more polar derivatives under alkaline sulfite conditions. Following these reactions, chloride ions and other polar compounds preferentially partition into the aqueous phase upon water addition. Subsequent phase separation and distillation remove the aqueous layer, thereby effectively eliminating chlorine from the organic (*R*)-carvone product.

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