

# Computer Aided Molecular Design: Replacements for the HFC Refrigerant R-134a using Global Optimisation

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## Abstract

— HFCs have a very high GWP and as such need to be phased out. Replacement refrigerant molecules for R-134a were investigated using computer-aided molecular design using constrained global optimisation techniques. Properties for potential molecules were estimated using group contribution theory. The mathematical formulation was implemented in GAMS and solved using the BARON solver. Integer cuts were used to find ten alternatives, all of which were similar to currently used refrigerants. HFOs were found to be an ideal solution with very low ODP and GWP. Further constraints were proposed on GWP, ODP, and flammability to improve the model.

**Key words:** *Integer cuts, global optimisation, BARON, computer-aided molecular design, HFCs, refrigeration, GAMS, R-134a*

## I. INTRODUCTION

CURRENTLY the global surface temperature of the earth is projected to increase by more than 5 °C by the year 2100 [1]. International agreements such as the Paris Agreement [2] have been signed by 196 nations who recognised the importance of preventing the increase of the global surface temperature by more than 1.5 °C. Among the largest greenhouse effect contributors is CO<sub>2</sub> however this was closely followed by emissions from CFCs which not only have stark global warming potential but also depleted the ozone layer. CFCs were made illegal and phased out by the Vienna Convention 1985, Montreal protocol 1987, and Clean Air Act of 1990. The alternative

refrigerants of choice became HFCs, which while less dangerous to the ozone layer, are still a highly potent class of greenhouse gases. The Kigali Amendment, to the Montreal Protocol, of 2016 was agreed upon by a number of signatories including China and it was ratified by all 196 UN member states. The Kigali Amendment set out to phase out the use of HFCs in industry. These are used extensively in refrigerators, aerosols, fire extinguishers, and air conditioning [3]. In this study we aim to find alternative molecules which can be used to replace HFCs, specifically R-134a (tetrafluoroethane), with similar or better physical properties and performance. To do this we make use of computer-aided molecular design (CAMD). Instead

of a trial-and-error laboratory synthesis approach where a molecule is synthesised and then its physical properties tested, we pre-select candidate molecules which fit the required physical properties for the desired molecule through computer-aided optimisation techniques. This saves time, and reduces the great expense of repeated laboratory testing. Molecular design is a highly challenging combinatorial problem. One has to construct a new molecule by choosing from  $N$  groups of atoms from a set of  $K$  potential groups. The total number of potential molecules explodes very quickly as  $K$  grows [4],

$$\sum_{i=2}^N \frac{(K+i-1)!}{i!(K-1)!}. \quad (1)$$

To circumvent this we make use of constrained optimisation where we set constraints for the physical properties. Often, these constraints are non-linear for features such as mechanical properties of a molecule [5], which leads to multiple local optima. The goal is to find globally optimal solutions which can be used to screen candidate molecules. We aim to use the methodology of group contribution methods as set out by Sahinidis et al. [6]. A vast array of molecules have been broken down into their constituent structural groups on a three order basis. This allowed Sahinidis et al. to characterise the contribution of each group of atoms in terms of thermodynamic properties to the overall molecule. This approach allows us to generate existing or even novel candidate molecules for the replacement of R-134a using an optimisation formulation such as the one outlined below,

$$\begin{aligned} \min & f(\mathbf{x}, \mathbf{n}) \\ \text{s.t.} & \mathbf{g}(\mathbf{x}, \mathbf{n}) \leq \mathbf{0} \\ & \mathbf{x} \in R^m, \mathbf{n} \in Z^N \end{aligned}$$

Here  $\mathbf{n}$  is a vector of integer variables they are used for modelling inclusionary and exclusionary

choices for groups;  $\mathbf{x}$  represents a vector of thermodynamic properties we are optimising for this investigation. Continuous constraints can be set through  $g(\mathbf{x}, \mathbf{n})$  and this can include ancillary objectives such as environmental safety, toxicity, and ozone depletion potential of molecules which are further discussed in the additional constraints section.

## II. PROBLEM STATEMENT & MOTIVATION

We designed a mixed integer non-linear problem (MINLP) motivated by the following aim: is it possible to find alternative refrigerant molecules to R-134a using branch-and-reduce global optimisation? Molecular design can be abstracted into graph theory where molecules are seen as a collection of atoms interlinked at vertices in a manner consistent with chemical bonding theory and physical property constraints.

We are aiming to find the most efficient candidate refrigerant possible. We are interested in running our refrigeration process with the smallest compressor such that our energy expenditure is minimised. This means we must minimise the volumetric flow rate,  $V_R$ , of refrigerant through the cycle i.e. minimise the amount of refrigerant used. It can be shown that,

$$V_R \approx \frac{Q}{H_{vap} - C_{p,L}(T_c - T_e)} \cdot V_m. \quad (2)$$

Where  $Q$  is the cooling load,  $H_v$  is the heat of vapourisation at 272 K,  $C_{p,L}$  is the liquid heat capacity at constant pressure and 272 K,  $V_m$  is the molar volume of the gas, and  $T_c$  and  $T_e$  represent the condenser and evaporator temperatures, respectively. Since we are trying to minimise  $V_R$  we need a large heat of vapourisation and small liquid heat capacity  $C_{p,L}$ . Alternatively, we can express the same principle through the optimisation of the following objective function,

$$\min \frac{C_{p,L}}{H_{v,272}}. \quad (3)$$

### III. METHODS

#### A. Design Space

The groups for the investigation were selected from those identified by Marrero and Gani [7] and were chosen to include those commonly found in refrigerants. Only first order groups were considered for this study, and no cyclic groups were selected to best replicate the small molecule size and simplicity of most common refrigerants. To prevent formation of CFCs due to their high ozone depleting potential (ODP), groups containing chlorine were excluded. While HFCs are highly undesirable, HFOs are promising alternative refrigerants which prevents the exclusion of fluorine containing groups. To ensure the model was solvable, groups were only included where there was no missing data on the parameters.

#### B. Property Estimation

The properties  $T_m$ ,  $T_b$ ,  $T_c$ ,  $H_v$ , and  $P_c$  were estimated using the group contribution method proposed by Marrero and Gani [7]. The equations in Table I were used to estimate the properties for each molecule based on the constituent groups.

TABLE I: Parameter Estimation

Parameter	Equation
Normal Melting Point, $T_m$	$T_m = T_{m0} \ln \sum_i N_i T_{mi}$
Normal Boiling Point, $T_b$	$T_b = T_{b0} \ln \sum_i N_i T_{bi}$
Critical Temperature, $T_c$	$T_c = T_{c0} \ln \sum_i N_i T_{ci}$
Standard Enthalpy of Vaporisation at 298K, $H_{v,298}$	$H_{v,298} = H_{v0} + \sum_i N_i H_{vi,298}$
Critical Pressure, $P_c$	$P_c = P_{c1} + (P_{c2} + \sum_i p_i)^{-2}$

This method gives the heat of vaporisation at 298 K. To obtain the value at 272 K the Watson equation is used to give the ratio between the latent heat of vaporisation at different temperatures [8]:

$$H_{v,272} = L_{v,298} \left[ \frac{T_c - 272}{T_c - 298} \right]^{0.38}. \quad (4)$$

Vapour pressure,  $P_v$ , is calculated using the Pitzer expansion [9],

$$\ln P_{vp_r} = f^{(0)} + \omega f^{(1)} + \omega^2 f^{(2)}. \quad (5)$$

This equation uses analytical expressions to provide the value of  $f^{(0)}$ ,  $f^{(1)}$ ,  $f^{(2)}$  and  $\omega$ . In this study the Ambrose and Walton expressions are used as shown,

$$f^{(0)} = \frac{-5.97616\tau + 1.29874\tau^{15}}{T_r} + \frac{-0.60394\tau^{2.5} - 1.06841\tau^5}{T_r}, \quad (6)$$

$$f^{(1)} = \frac{-5.03365\tau + 1.11505\tau^{15}}{T_r} + \frac{-5.41217\tau^{25} - 7.46628\tau^5}{T_r}, \quad (7)$$

$$f^{(2)} = \frac{-0.64771\tau + 2.41539\tau^{15}}{T_r} + \frac{-4.26979\tau^{25} + 3.25259\tau^5}{T_r}, \quad (8)$$

where  $\tau$  and  $T_r$  depend on temperature:

$$\tau = 1 - T_r, \quad (9)$$

$$T_r = \frac{T}{T_c}. \quad (10)$$

The acentric factor,  $\omega$ , is

$$\omega = -\frac{\ln(P_c/1.01325) + f^{(0)}(T_{br})}{f^{(1)}(T_{br})}, \quad (11)$$

with  $T_{br}$  calculated using

$$T_{br} = \frac{T_b}{T_c}. \quad (12)$$

This calculation is done at the two required temperatures 272 K and 316 K.

The heat capacity for each group,  $C_{pi}$ , was calculated from the contributions reported by Benson et al. [10]. The groups used in that report were different from those used by Marrero and Gani and in this study, hence the estimates for heat capacity were calculated by summing the contribution from each atom. For example, the heat capacity for

the group CH<sub>2</sub>NH was calculated by summing the heat capacity recorded for C–(N)(C)(H)<sub>2</sub> and N–(C)<sub>2</sub>(H). Each atom required full connectivity in the model from Benson et al., so to combine these it was assumed that any free bonds in a group represented a bond to a C atom, as this is most likely to be the atom in a group with a free valency. Once the contribution for each group was obtained,

$$C_{p,L} = \sum_i N_i C_{pi} \quad (13)$$

was used to estimate the heat capacity of the molecule.

### C. Problem Formulation

#### 1) Physical constraints

Physical constraints for the model arise from the desired process and restrict the domain to only include suitable molecules. Pressure in the system should be greater than atmospheric to prevent air from leaking into the system, and a maximum pressure rise of about ten times is suggested [6]. The highest pressure in the system will be in the condenser and the lowest pressure in the evaporator, both of which are determined by the vapour pressure of the refrigerant.

$$P_{v,272} \geq 1.1 \quad (14)$$

$$P_{v,316} \leq 14 \quad (15)$$

show the constraints which ensure the system pressure is between 1.1 bar and 14 bar.

Additional constraints consider that the performance of the new refrigerant should be superior to that of R-134a. This leads to constraints on heat capacity and latent heat of vaporisation at the evaporating temperature,

$$H_{v,T_e} \geq 20.33, \quad (16)$$

$$C_{p,L} \leq 143.9. \quad (17)$$

The data for R-134a is obtained from literature [11]. Furthermore, to ensure the refrigerant can flow through the system it is desired that it is in the liquid or gaseous phase at the process temperatures. Equation 18 constrains the model such that any candidate molecules must not be solid at the evaporating temperature of 272 K,

$$T_m \leq 272. \quad (18)$$

#### 2) Structural Constraints

The active region must be constrained further to only allow combinations of groups that leads to the formation of feasible molecules. This is achieved using the free valency of each group,  $v_i$ , which represents how many bonds it can form. The structural constraints are adapted from Sahinidis et al. [6], without the considerations for cyclic groups as these are not part of the active set. Each group is specified to form single bonds only as any double bonds would be accounted for by a different group. To ensure there are no free bonds in the molecule, the sum of the valencies must be even, shown for an acyclic molecule by

$$\left( \sum_i (2 - v_i) N_i \right) - 2 = 0. \quad (19)$$

The minimum number of bonds formed must be at least equal to the number of groups minus one, which gives

$$\sum_i N_i v_i \geq 2 \left( \sum_i N_i - 1 \right), \quad (20)$$

after noting that the number of bonds is half of the sum of the valencies. The maximum number of bonds formed cannot exceed that of a complete graph where all groups are connected,

$$\sum_i N_i v_i \leq \left( \sum_i N_i \right) \left( \sum_i N_i - 1 \right). \quad (21)$$

To prevent adjacent groups from bonding together twice the constraint,

$$N_j (v_j - 1) + 2 - \sum_{i \in G} N_i \leq 0, \forall j \in G, \quad (22)$$

must be implemented where  $G$  is the full set of groups. To further limit the design space the maximum number of total groups is set to 15,

$$\sum_i N_i \leq 15. \quad (23)$$

The minimum number of groups is also restricted to 2,

$$\sum_i N_i \geq 2. \quad (24)$$

#### D. Other Constraints

To prevent the formation of HFCs and ensure fluorine is only present in HFOs a constraint using the big-M method was added

$$\sum_F N_i \leq 15 \sum_O N_i \quad (25)$$

$F, O \subseteq G$

F and O are subsets of G including the groups with fluorine and the groups with C=C bonds, respectively. When there are no C=C containing groups in the molecule, fluorine containing groups are not permitted; when there is at least one C=C containing group the constraint allows the rest of the possible groups in the molecule to contain fluorine. Upon recommendation from Sahinidis [6], the maximum possible number of any group can be set at five without restricting possible solutions,

$$N_i \leq 5. \quad (26)$$

A binary representation of each possible integer  $N_i$  is identified in the model by,

$$N_i = \sum_k 2^{k-1} y_{k,i}. \quad (27)$$

As the largest integer required is five the required indexes are  $k \in \{1, 2, 3\}$ . The binary variables,  $y_{i,k}$ , are used to make integer cuts which can make certain solutions infeasible. The general equation for an integer cut is

$$\sum_{i \in NZ} y_i - \sum_{i \in Z} y_i \leq |NZ| - 1, \quad (28)$$

where  $NZ$  is the set of variables equal to 1 in the solution and  $Z$  is the set of variables equal to zero.

#### E. Model Implementation

The mathematical formulation was implemented in GAMS to minimise the objective function as shown in Equation 3. Bounds were set on the physical parameters to ensure they were positive. The solver BARON was used to identify the global solution in terms of groups included, from which the candidate molecule was identified each iteration. The properties as predicted by the model were then recorded. Integer cuts were used to eliminate each incumbent solution to give the ten different candidate molecules.

### IV. RESULTS & DISCUSSION

We have determined ten alternative candidate refrigerant molecules for the replacement of R-134a using our global optimisation model. The candidate selections are presented in Table II. The selected molecules fall into four types: alkenes, hydrofluoro-olefins (HFO), amines, and ethers. The candidate molecule with the lowest objective function was 3-fluoropropene, a HFO. This is promising because HFOs are an active field of research for the replacement of HFCs because of their "super low GWP", [12]. While 3-fluoropropene itself is not currently used as a refrigerant a similar molecule, fluoroethylene more commonly referred to as R-1141, is in fact used in refrigeration systems and shows favourable thermodynamic performance and it has a low GWP and ODP. Similarly, one more HFO was selected; 3,3,3-trifluoropropene, which while not used as a refrigerant itself also has a similar molecule which is used as a refrigerant, R-1234yf (2,3,3,3-tetrafluoropropene). Alkenes, amines, and ethers are also common refrigerant molecules. This is a

good indication of these molecules being suitable alternatives to R-134a.

The only molecule which has known carcinogenic effects is 2-butadiene while 3,3,3-trifluoropropene, methyl ethyl ether, but-1-ene, and trimethyl amine present asphyxiation and irritation risks when inhaled or in close contact with skin. None of the candidate molecules are considered to be ozone depleting substances according to the United Environmental Protection Agency [13]. We also considered the candidate molecules in terms of their global warming potential and found that their GWP values were all very low and approximately 400 times lower than R-134a based on the GWP of similar molecules [14].

When executing integer cuts we encountered a repeated molecule after seven cuts, methyl ethyl ether. This molecule was made up from two different combinations of similar groups. The first methyl ethyl ether was made from two CH<sub>3</sub> and one CH<sub>2</sub>O group. Whereas, the second one after integer cut seven was made from one CH<sub>3</sub>O, CH<sub>2</sub>, and one CH<sub>3</sub> group. When comparing the thermodynamic properties of these two repeats we find they are not identical. This shows that there is a noticeable error in the properties when different groups are selected to make the same molecule. The most notable difference was found in the vapour pressure, with the repeated methyl ethyl ether having a 50% lower value than the first iteration.

## V. ADDITIONAL CONSTRAINTS

When selecting candidate molecules based on the optimisation model we considered physical bonding constraints which would prevent infeasible molecules from being selected. However, thermodynamic properties and physical bonding properties based on VESPR theory do not account for important physical features such as toxicity, flammability, GWP, ODP, and other environmen-

TABLE II: Candidate Refrigerant Molecules

Name	Formula	Molecule
3-fluoropropene	$\text{CH}_2=\text{CHCH}_2\text{F}$	
Dimethylamine	$\text{CH}_3\text{NHCH}_3$	
Methoxyethene	$\text{CH}_3\text{OCH}_2=\text{CH}_2$	
3,3,3-trifluoropropene	$\text{CH}_2\text{CH}_2\text{CF}_3$	
Methyl ethyl ether	$\text{CH}_3\text{CH}_2\text{OCH}_3$	
But-1,3-diene	$\text{CH}_2=\text{CHCH}_2=\text{CH}_2$	
But-2-ene	$\text{CH}_3\text{CH}_2=\text{CHCH}_3$	
But-1-ene	$\text{CH}_3\text{CH}_2\text{CH}_2=\text{CH}_2$	
Trimethylamine	$\text{N}(\text{CH}_3)_3$	
2-methylpropene	$\text{CH}_2=\text{C}(\text{CH}_3)_2$	

tal safety constraints. We have developed three further constraints which can be applied to the optimisation problem to filter out molecules which even though they may fulfil the thermodynamic criteria would be poor candidates in real world use-cases.

### A. Ozone Depletion Potential

The main reason why CFCs were phased out was their significant danger to the ozone layer. HFCs pose a much smaller threat with a very low ODP. In particular R-134a has an OPD of *zero*. As such it is important that we screen the design space of molecules for combinations which lead to an ODP

of zero or very close to zero. This would require a group contribution breakdown as a function of ODP. The mathematical formulation for this would lead to an equality constraint which must be added in the form of,

$$g_1(\mathbf{x}, \mathbf{n}) = 0. \quad (29)$$

Where  $g_1(\mathbf{x}, \mathbf{n})$  represents the ODP measure for each candidate molecule which we want to keep to zero. Correlations for ODP values have been reported for one to two carbon compounds [15]. Compounds without chlorine have an ODP rating of close to zero and generally haloalkanes have non-zero ODP values because of the longer and weaker C–F bond. We can set the ODP value of all group contributions to zero except for the ones which contain fluorine. We can also constrain it so that if a HFO is formed the ODP is set to zero since HFOs have been shown to have almost no impact on the ozone layer [12].

### B. Global Warming Potential

The reason HFCs are being phased out is because of their severe global warming potential. The GWP of R-134a is 1430 [16] which is almost 1500 times that of CO<sub>2</sub>. It is imperative that we should constrain the universe of possible candidate molecules to ones which have a GWP lower than R-134a. The formulation which could be added to the optimisation problem would be,

$$g_2(\mathbf{x}, \mathbf{n}) \leq 1430. \quad (30)$$

This forms a continuous inequality constraint which has to be added to the problem statement. For this to work we would have to find the group contributions of each group of atoms to the global warming potential index. The challenge with this is GWP is a highly complex function of atmospheric interactions with the molecule, atmospheric abundance of the molecule, and infra-red absorption characteristics of the molecule in the atmosphere.

GWP varies for each molecule depending on the atmospheric conditions. There are two ways around this problem; firstly, one could determine the mean group contributions of atoms to GWP for a set of common atmospheric conditions and then one could use these values in the optimisation model we have created. Alternatively, radiative transfer of group contributions can be considered as a proxy for GWP as shown by Zhang et al. [17].

### C. Flammability

R-134a, according to ASHRAE is classified as A1 [18], which means it is not flammable enough to propagate a flame and it is not toxic. All of the candidate molecules we have found have substantial flammable potential. As a third safety constraint we can impose a limit on the flammability potential of the candidate molecules. We can use ASHRAE guidelines together with R-134a as a reference so that we restrict the universe of molecules we are searching to ones which are as flammable or less than R-134a. This would involve the following two conditions,

$$\text{LFL} > 100 \text{ g m}^{-3} \quad \& \quad \Delta H_{\text{comb}} < 19 \text{ MJ}. \quad (31)$$

The reason we have considered this is because R-134a is frequently used in car ACs and a lot of these units are not properly disposed of, which means the refrigerant gas can escape, and or cause damage if heated up on a landfill site if it is highly flammable. We can approximate the heats of combustion,  $\Delta H_{\text{comb}}$ , for the molecules using the heats of formation provided by Marrero and Gani [7] and the lower flammability limits (LFL) can be approximated by considering how much air usually leaks into the refrigeration cycle - this would be the greatest source of error as these values are not well documented.

## VI. CONCLUSION

We found ten alternative candidate molecules, all of which satisfy the thermodynamic and process requirements of the refrigerant. All of these candidates are similar to molecules which are already being used as refrigerants and this, along with their GWPs and ODPs, reinforces their suitability as replacements for R-134a. While, the property estimation was not completely accurate, these molecules have been identified as good starting points for further laboratory investigation into their physical properties as well as real world performance as refrigerant molecules. Our investigation has shown that this topic of research can benefit from further studies using a CAMD approach with more rigorous property estimation, using second and third order groups, and further constraints such as the aforementioned examples. Our model yielded known compounds, however an adapted formulation of the model with more integer cuts could potentially lead to novel compounds being discovered.

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