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Synthesis and crystallization procedure of piperidin-4-one and its derivatives: An update

Arulraj Ramalingam [a,*]

[a] *Department of Electrical and Computer Engineering, National University of Singapore, 117 583, Singapore.*

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ABSTRACT

Piperidine is a heterocyclic chemical molecule that is forming by hydrogenating pyridine. In natural and pharmaceutically active drugs, the piperidine ring is an essential molecular component. Several crystal structures of piperidine-4-ones and their derivatives are reported for their medicinal value. While several methods of piperidin-4-one crystallization have been developed to obtain a crystal structure, novel approaches are still needed. A review of the synthesis and crystallization procedure of piperidin-4-ones and its derivatives is outlined in this review paper.

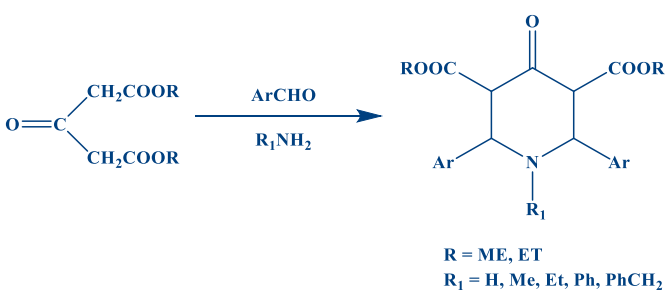
1. Introduction

Over the last decade, clinical and preclinical studies have mentioned thousands of piperidine compounds. Considerable attention has also been drawn to the importance of analgesic and anti-inflammatory activities containing compounds and the synthesis of piperidine-4-one derivatives [1]. There are many biological activities of piperidine derivatives, such as analgesic, antihypertensive, antiviral central nervous system depressant, antibacterial, antifungal, etc. [2-6]. Watson et al. reported that there were thousands of piperidine compounds mentioned in clinical and preclinical studies over the last 10 years [7].

There are vital biological profiles of nitrogen-containing heterocycles. For example, the sub-structure of piperidine is ubiquitous. Structural features of many alkaloids, natural products, and candidates for drugs [8]. Crystallization is a method used for the purification of solid compounds by chemists. It is one of the fundamental processes that must be mastered by and chemist to become competent in the laboratory. Impurities are removed from the growing crystals and filtration will isolate the pure solid crystals from the dissolved impurities. While several piperidine-4-ones and its derivatives crystallization techniques have been developed to obtain a crystal structure.

2. Synthesis of piperidine-4-ones by Mannich condensation

The Mannich condensation reaction between substituted aromatic aldehydes, ethyl methyl ketone, and ammonium acetate in ethanol medium ware synthesized as substituted 4-piperidones. Mannich first recognized the formation of β-amino carbonyl compounds (Mannich bases) from the reaction of an active methylene compound with formaldehyde and amine [9]. Baliah et al [10-15] developed an elegant 2, 6-diphenylpiperidine-4-ones synthesis method based on the earlier work of Petrenko-Kritschenko et al. [16-19]. The previous reaction involved the condensation of an acetone dicarboxylic acid ester with an aromatic aldehyde and ammonia or a primary amine, resulting in the formation of 2,6-diaryl-4oxopiperidine-3,5-dicarboxylate or its N-substituted derivatives as shows in scheme 1.



Scheme 1: Synthesis of piperidine-4-ones by Mannich condensation

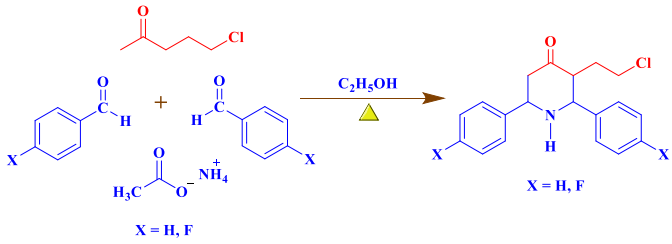
* Corresponding author. Tel.: +65 94794145; e-mail: rarulraj108@gmail.com

3. The general procedure of recrystallization of non-volatile organic solids

The most significant method of purifying non-volatile organic solids is recrystallization. Recrystallization involves dissolving in a suitable hot organic solvent the substance to be purified. The solution saturated with the solvent and the solvent crystallizes out as the solvent cools. Impurity material is removed from the crystal lattice as the crystal forms, thus completing the purification process. It is then possible to extract, wash, and dry the crystals. Typically, chemists decide the solvent for recrystallization. At low temperatures, like room temperature, the solvent does not dissolve the compound, but at high temperatures, it must dissolve the compounds. To rid its lattice of impurities, the solute must dissolve, but must not stay dissolved at room temperature. Except at room temperature, if the solvent readily dissolves the impurities, then the impurities in the forming crystal lattice will not be trapped but will remain dissolved in the solvent. If the impurities do not degrade even at high temperatures, so gravity filtration will effectively eliminate them. Only when the solvent is heated can Solute dissolve. When too much solvent is added, upon freezing, the solution will not be saturated, and no crystals will form. The solution needs to be decolorized with charcoal if the solvent were supposed to be white in its pure solid-state. It includes the dissolved solution to continuously return to room temperature with the hot solution. The slower the cooling process, the less likely it is to trap impurities in the crystal lattice that forms

4. Piperidine-4-one compounds recrystallized with ethanol as a solvent

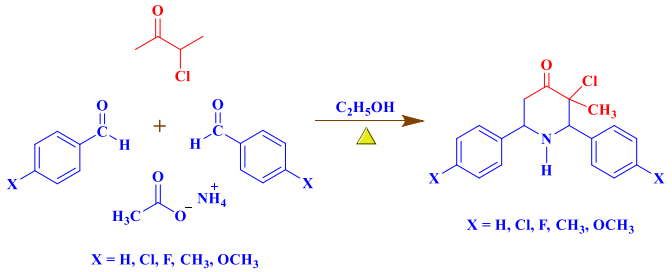
Crystallization methods are used to purify a synthesized organic compound to get good crystals without impurities. In the crystallization technique, purified ethanol or absolute ethanol is one of the solvents for purifying. The 1-chloroacetyl-2,6-bis(2-methoxyphenyl)-3,5-dimethylpiperidin-4-one compound reported by Aridoss *et al* [20] has been recrystallized using distilled ethanol. In the reported compound, $C_{23}H_{26}ClNO_4$, the piperidine ring adopts a boat conformation with the two aromatic rings are perpendicular to each other. Likewise, the two crystal compounds recrystallized by distilled ethanol such as 3-(2-chloroethyl)-r-2,c-6-diphenylpiperidine-4-one, $C_{19}H_{20}ClNO$, and 3-(2-chloroethyl)-r-2,c-6-bis(4-fluorophenyl)piperidine-4-one, $C_{19}H_{18}ClF_2NO$, were reported by Rajkumar *et al*. [21] In the reported crystal, $C_{19}H_{20}ClNO$, the piperidone ring adopts a chair conformation, whereas a slightly distorted chair conformation formed in $C_{19}H_{18}ClF_2NO$ as shows in scheme 2.



Scheme 2: Synthesis of some 3-(2-chloroethyl)-r-2,c-6-diphenylpiperidine-4-ones

The synthesized compound some 3-chloro-3-methyl-r(2),c(6)-diphenylpiperidine-4-ones, were recrystallized using distilled ethanol, and its reported by Arulraj *et al* [22-26] as shows in scheme 3.

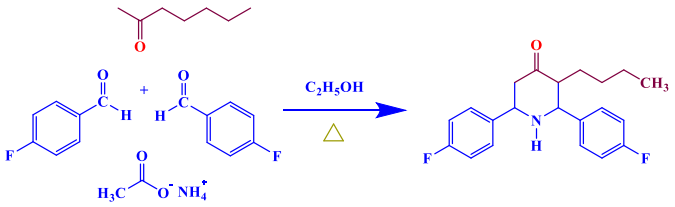
The synthesised and reported crystal structure 3-chloro-3-methyl-r-2,c-6-diphenylpiperidin-4-one, $C_{18}H_{18}ClNO$, 3-chloro-3-methyl-*r*-2,*c*-6-*di*-p-tolylpiperidin-4-one, $C_{20}H_{22}ClNO$, and 3-chloro-3-methyl-*r*-2,*c*-6-bis(4-chlorophenyl)-piperidin-4-one, $C_{18}H_{16}Cl_3NO$, the piperidine ring adopts a chair conformation. Whereas the 3-chloro-*r*-2,*c*-6-bis(4-fluorophenyl)-3-methylpiperidin-4-one , $C_{18}H_{16}ClF_2NO$, contains one independent molecule in the asymmetric unit, with the piperidin-4-one ring adopting a slightly distorted chair conformation and an equatorial orientation of all the substituents except chlorine. In the methoxy substituted crystal structure 3-chloro-3-methyl-r(2),c(6)-bis(p-methoxyphenyl)piperidin-4-one, $C_{20}H_{22}ClNO_3$ the piperidin-4-one ring adopts a slightly distorted chair conformation and an equatorial orientation of all its substituents except for chlorine which is axially located.



Scheme 3. Synthetic scheme of some 3-chloro-3-methyl-*r*(2),*c*(6)-diphenylpiperidine-4-ones

Anitha *et al* [27] synthesised and reported the 3-butyl-2,6-bis(4-fluorophenyl)piperidin-4-one, $C_{21}H_{23}F_2NO$ with recrystallized with absolute ethanol. The reported crystal compounds consist of two fluorophenyl groups and one butyl group equatorially oriented on a piperidine ring, which adopts a chair conformation as shown in scheme 4.

The reported compounds are crystallised with ethanol. The reported crystal compounds exist in the normal chair confirmation as shown in the scheme 15.



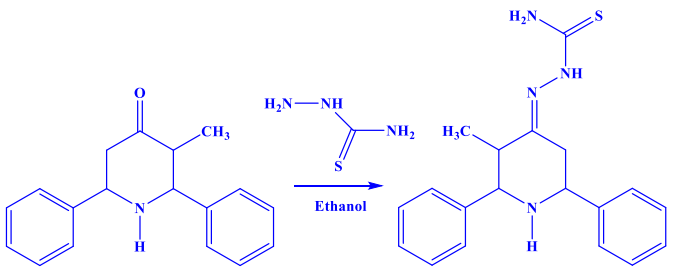
Scheme 4. Synthetic scheme of 3-butyl-2,6-bis(4-fluorophenyl)piperidin-4-one.

5. Piperidine-4-one crystals recrystallized with ethanol-ethyl acetate and benzene-petroleum ether mixture as a solvent

The 2,6-diaryl-3-(4-arylthio)piperidin-4-one series was synthesised, recrystallized and reported by Murugesan *et al* [28] from a mixture of ethanol-ethyl acetate. All piperidine rings occur in chair conformation with the equatorially oriented 2,6-diaryl groups. Manimekalai *et al* [29] reported some N-acyl-t(3)-isopropyl-r(2),c(6)-bis-(2'furyl)piperidin-4-ones compounds were synthesized and recrystallized using benzene-petroleum ether mixture. The spectral evidence of the compounds indicates that the synthesized compounds occur in alternate chair form or boat form. Manjula *et al* [30] synthesized and reported the 2,6-diphenyl-3-(prop-2-en-1-yl)piperidin-4-one, $C_{20}H_{21}NO$ with recrystallized using benzene-petroleum ether mixture. The piperidine ring of the reported compound adopts a chair conformation. The substituent adopts an equatorial orientation.

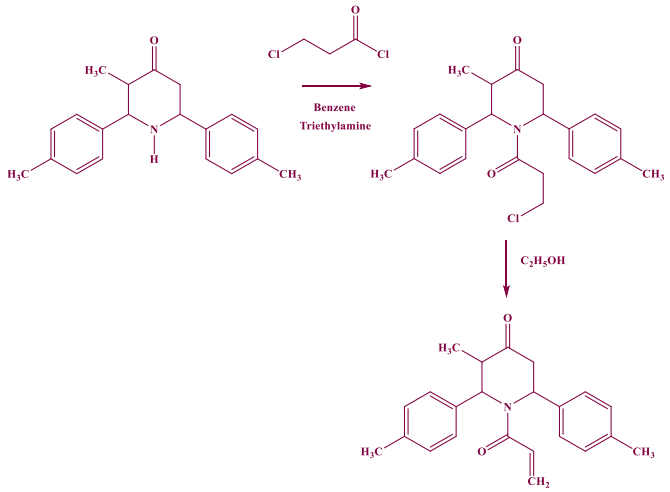
6. Recrystallization procedure of piperidine-4-one derivative compounds

The compound r-2,c-6-Bis(4-chlorophenyl)-t-3-isopropyl-1-nitrosopiperidin-4-one, $C_{20}H_{20}Cl_2N_2O_2$ were recrystallized from distilled ethanol and the piperidine ring adopts a chair conformation and the nitroso group at position 1 has a bisectional orientation reported by Gayathri *et al* [31]. The synthesised compound t-3-methyl-r-2,c-6-diphenylpiperidin-4-one thiosemicarbazone, $C_{38}H_{44}N_8S_2{\cdot}2(C_2H_3N)$ were recrystallized from acetonitrile reported by Sampath *et al* [32]. The synthesised compound adopts chair conformations by the piperidine rings. The planar phenyl rings of the piperidine ring are equatorially oriented at 2,6-positions as shows in Scheme 5.



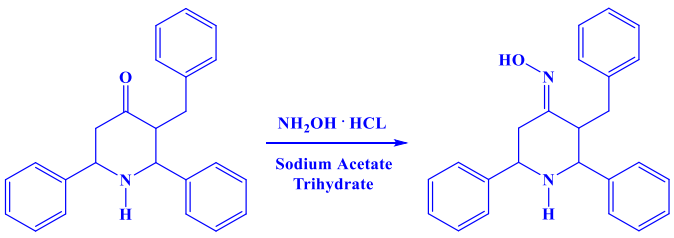
Scheme 5: Synthesis of t-3-methyl-r-2,c-6-diphenylpiperidin-4-one thiosemicarbazone

The 1-acryloyl-3-methyl-2,6-dip-tolylpiperidine-4-one, $C_{24}H_{27}NO_3$ compound synthesised and recrystallized by slow evaporation method with ethanol reported by Lakshminarayana *et al* [33]. The spectral evidence shows that the piperidine ring adopts by twist boat conformations and the molecule crystallizes in the monoclinic crystal class with C2/c space group. The synthetic scheme of the crystal compound shows in scheme 6.



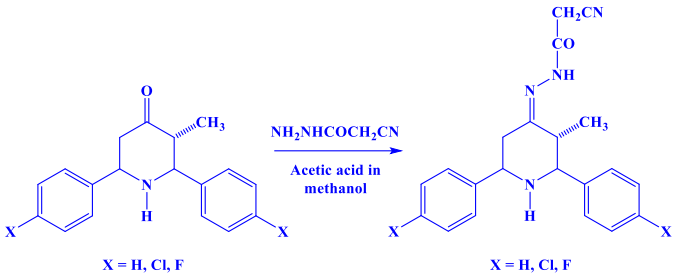
Scheme 6: Synthesis of 1-acryloyl-3-methyl-2,6-dip-tolylpiperidine-4-one

Arulraj *et al* [34-35] synthesised and reported the t-3-benzyl-r-2,c-6-diphenylpiperidin-4-one, $C_{24}H_{23}NO$ and t-3-benzyl-r-2,c-6-diphenylpiperidin-4-one oxime, $C_{24}H_{24}N_2O$ recrystallized with distilled ethanol. The parent compound $C_{24}H_{23}NO$ contains two crystallographically independent molecules (1 and 2). In both molecules, the piperidine rings adopt a chair conformation, and the phenyl rings and the benzyl group substituents are attached equatorially. Whereas the oxime substituted compounds spectral data shows the piperidine ring adopts a slightly distorted chair conformation. The other substituents of the phenyl rings and the benzyl group are attached equatorial orientation as shown in scheme 7.



Scheme 7: Synthesis of t-3-Benzyl-r-2,c-6-diphenylpiperidin-4-one oxime

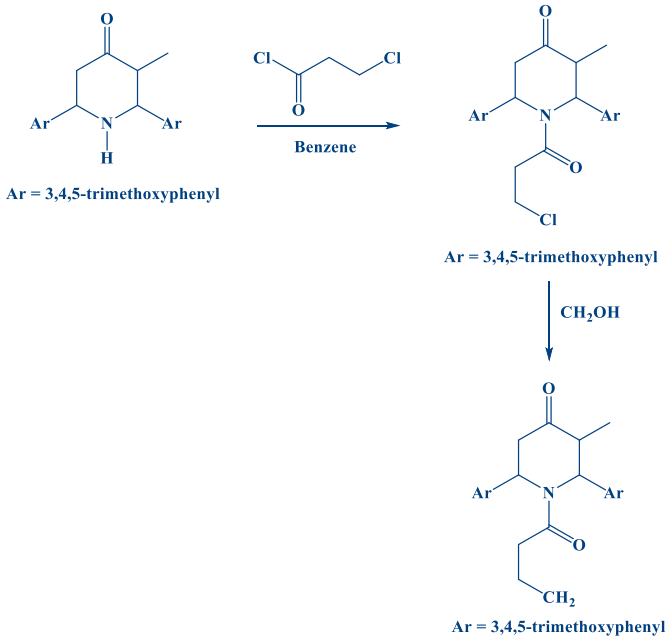
Another interesting compound 3-octyl-4-oxo-2,6-bis(3,4,5-trimethoxyphenyl)-piperidinium chloride, $C_{31}H_{46}NO_7^+ \cdot Cl^-$ synthesised, recrystallized from ethanol and reported by Rubina *et al* [36]. In the molecule, a chair conformation is adopted by the piperidine ring, and the trimethoxy-substituted benzene rings and octyl chains are equatorially arranged. Sivakumar *et al* [37] synthesized and reported the some r(2),c(6)-diarylpiperidin-4-one cyanoaceticacid hydrazones with recrystallized with methanol. The reported crystal compounds adopt chair conformation with the equatorial orientations of all substituents are as shown in scheme 8.



Scheme 8: Synthesis of some r(2),c(6)-diarylpiperidin-4-one cyanoaceticacid hydrazones

Gnanendra *et al* [38] synthesized the 1-acryloyl-3-methyl-2,6-bis(3,4,5-trimethoxyphenyl) piperidine-4-one, $C_{27}H_{33}NO_8$ recrystallized by slow evaporation with ethanol. The reported crystal compound crystallized in the orthorhombic crystal class under the *Pbca* space group. The piperidine ring adopts a twist boat conformation for the reported compound as shown in scheme 9. Raghuvarman *et al* [39] synthesised the (E)-(3-ethyl-1-methyl-2,6-diphenylpiperidin-4-ylidene)amino phenyl carbonate $C_{27}H_{28}N_2O_3$, and (E)-(3-isopropyl-1-methyl-2,6-diphenylpiperidin-4-ylidene)amino phenyl carbonate, $C_{28}H_{30}N_2O_3$ recrystallized by DMF–water mixture (9:1) to get colourless block-like crystals. In both crystal structure shows the piperidine rings adopt chair conformations with the attached phenyl rings almost normal to their mean planes. Sun *et al* [40] synthesised and reported (3E,5E)-3,5-bis(3-nitrobenzylidene)-1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-one-dichloromethane (2/1), $C_{53}H_{38}Cl_2F_6N_6O_{14}S_2$ recrystallized by dichloromethane/methanol (1:1, v/v) to get light yellow crystals of the reported crystal compound.

Amala *et al* [41] synthesised and reported the some 3-ethyl-5-methyl-2,6-diarylpiperidin-4-on-1-ium picrates recrystallized using ethanol. The crystallographic data of the synthesised crystal compounds revealed that the structures adopts a chair conformation as shown in scheme 10. Selvaraju *et al* [42] synthesised and reported the N-formyl-t(3)-ethyl-r(2),c(6)-di(2'-furyl)piperidin-4-one, N-acetyl-t(3)-ethyl-r(2),c(6)-di(2'-furayl)piperidin-4-one, N-propanoyl-t(3)-ethyl-r(2),c(6)-di(2'-furyl) piperidin-4-one and N-benzoyl-t(3)-ethyl-r(2),c(6)-di(2'-furyl)piperidin-4-one were recrystallized from benzene-petroleum ether mixture.



Scheme 9: Synthesis of some 1-acryloyl-3-methyl-2,6-bis(3,4,5-trimethoxyphenyl) piperidine-4-one.

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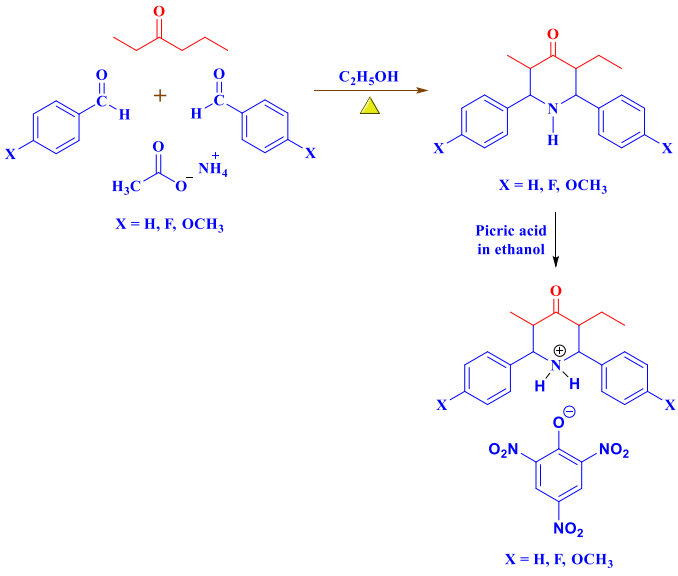
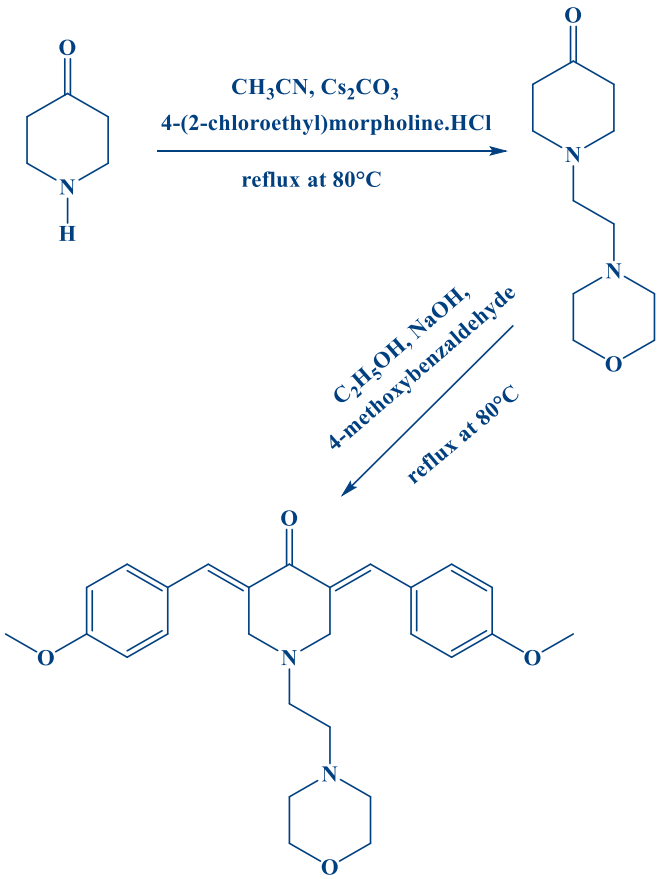


Scheme 10: Synthesis of some 3-ethyl-5-methyl-2,6-diarylpiperidin-4-on-1-ium picrates

Kuswardani *et al* [43] synthesised and reported the 3,5-bis((E)-4-methoxybenzylidene)-1-(2-morpholinoethyl)piperidin-4-one, $C_{27}H_{33}N_2O_4$ crystal compound and its recrystallized from methanol as shown in scheme 11. Thenmozhi *et al* [44] synthesised and reported the 1-chloroacetyl-r-2,c-6-bis(4-

The reported compounds are crystallised with ethanol. The reported crystal compounds exist in the normal chair confirmation as shown in the scheme 15.

methoxyphenyl)-c-3,t-3-dimethylpiperidin-4-one, $C_{23}H_{26}ClNO_4$ purified by recrystallization from petroleum ether (60-80°C). The piperidine ring adopts a distorted boat conformation within the observed crystal structure. At the 2 and 6 positions of the piperidine ring, two methoxyphenyl groups are axially and equatorially. Thenmozhi *et al* [45] synthesised and reported the 1-dichloroacetyl-r-2,c-6-bis(4-methoxyphenyl)-c-3,t-3-dimethylpiperidin-4-one, $C_{23}H_{25}Cl_2NO_4$ crystal compound and its recrystallized from ethanol. The reported crystal structure shows that the piperidine ring adopts a distorted boat conformation.

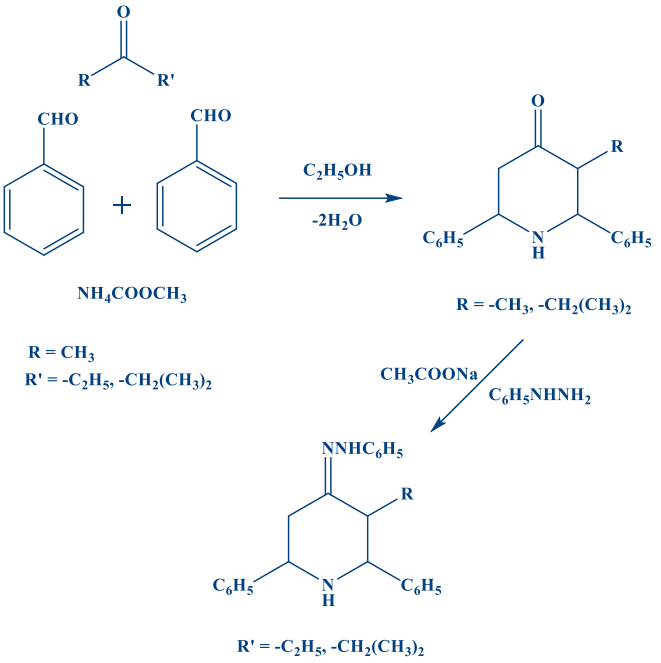


Scheme 11: Synthesis of 3,5-Bis((E)-4-methoxybenzylidene)-1-(2-morpholinoethyl)piperidin-4-one

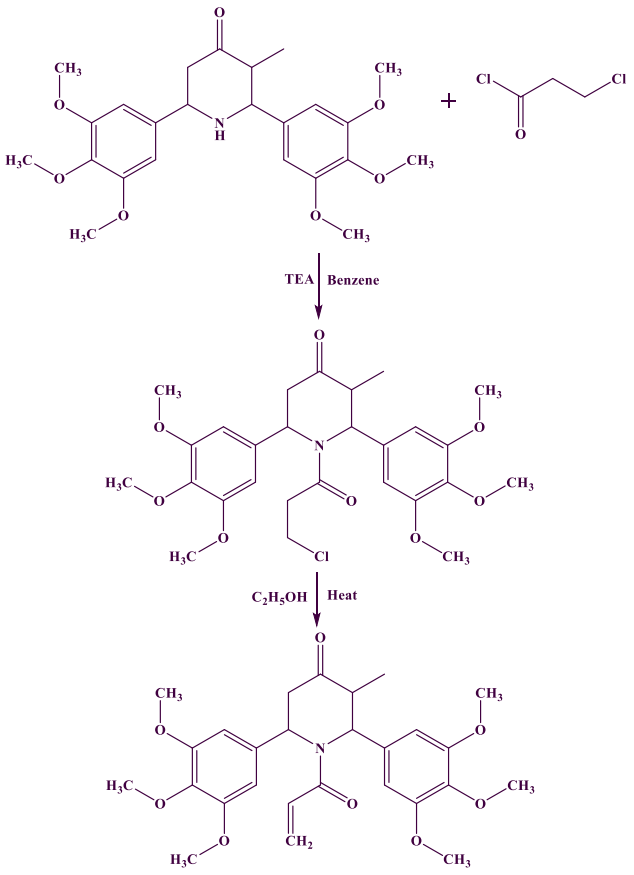
ALkhafaji *et al* [46] synthesised and reported the series of 2,6-bis(4-Subtituetphenyl)-3-methylpiperidin-4-one. The reported crystal compounds are recrystallized with 95% ethanol.

Rajesh *et al* [47] synthesised and reported the phenyl hydrazine derivatives of 2,6-diphenylpiperidin-4-ones, crystal compound and its recrystallized from absolute ethanol as shown in scheme 12.

Gnanendra *et al* [48] synthesised and reported the 1-Acryloyl-3-methyl-2,6-bis(3,4,5-trimethoxyphenyl)piperidine-4-one, $C_{27}H_{33}NO_8$ crystal compound. It was recrystallized from ethanol and its crystallizes in the orthorhombic crystal class. The reported crystal structure shows that the piperidine ring adopts a twist boat conformation as shown in scheme 13.

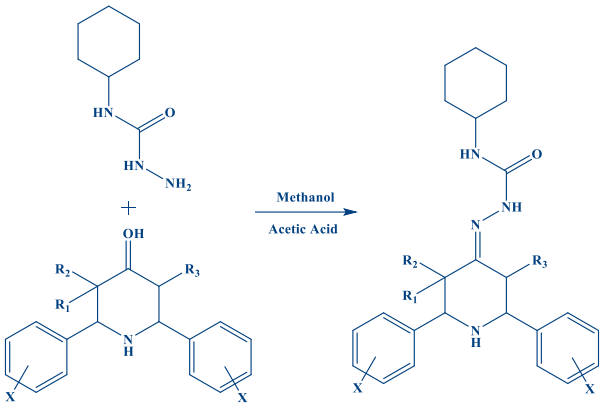


Scheme 12: Synthesis of phenyl hydrazine derivatives of 2,6-diphenylpiperidin-4-ones



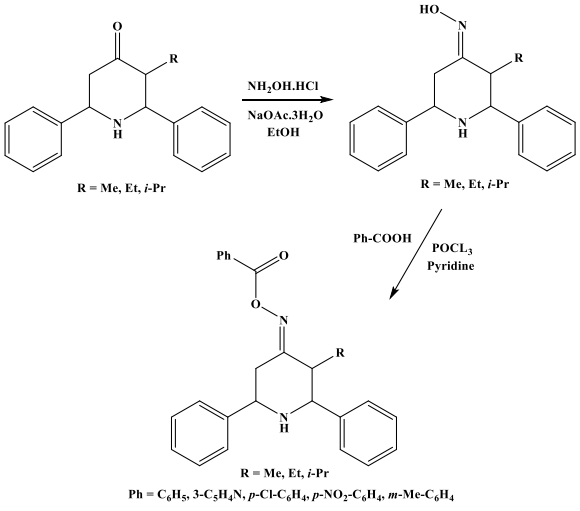
Scheme 13: Synthesis of 1-Acryloyl-3-methyl-2,6-bis(3,4,5-trimethoxyphenyl)piperidine-4-one

Anand *et al* [49] synthesised and reported the series of 2,6-diarylpiperidin-4-one *N*(4')-cyclohexylsemicarbazones. All the synthesised compounds are recrystallized with ethanol. The reported compounds are existing in chair conformation with the diequatorial orientation of bulky aryl substituents as shown in the scheme 14.



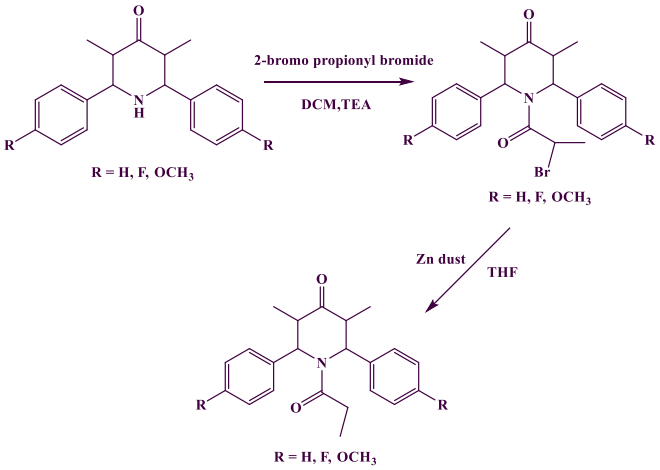
Scheme 14: Synthesis of 1-Acryloyl-3-methyl-2,6-bis(3,4,5-trimethoxyphenyl)piperidine-4-one

Sun *et al* [50] synthesised and reported the crystal structure of (3E,5E)-3,5-bis(3-nitrobenzylidene)-1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-one dichloromethane (2/1), $C_{53}H_{38}Cl_2F_6N_6O_{14}S_2$. The reported crystal structure was recrystallized from dichloromethane/methanol (1:1, v/v) to get light yellow crystals. Sundaresan *et al* [51] synthesised and reported the crystal structure of N-Benzyl piperidin 4-one oxime derivative and recrystallized from methanol. Gokula Krishnan *et al* [52] synthesised and reported the crystal structure of some novel 3-alkyl-2,6-diphenylpiperidin-4-one oxime esters compounds.



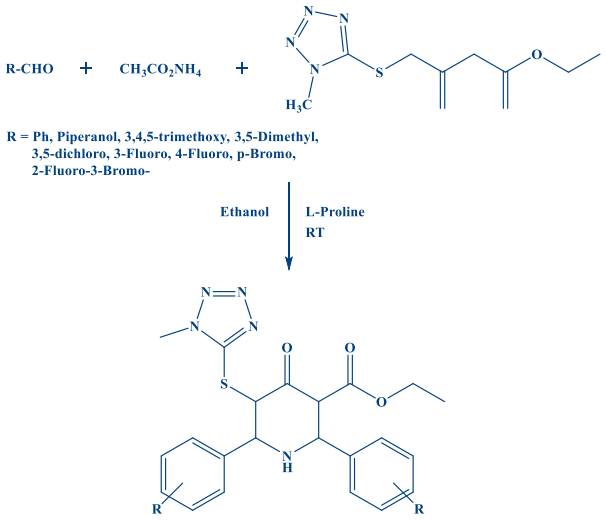
Scheme 15. Synthesis of 3-alkyl-2,6-diphenylpiperidin-4-one oxime esters.

Suresh *et al* [53] synthesised and reported the crystal structure of 3,5-dimethyl-2,6-diphenyl-1-propionyl-piperidin-4-one compounds. The reported compounds are crystallised with methanol. The reported crystal compound exist in the piperidine ring adopts a slightly disordered twist-boat confirmation as shown in the scheme 16.



Scheme 16. Synthesis of 3,5-Dimethyl-2,6-diphenyl-1-propionyl-piperidin-4-one

Srikanth *et al* [54] synthesised and reported some Ethyl 5-(1-methyl-1h-tetrazol-5-ylthio)-4-oxo-2,6-substituted diphenylpiperidine-3-carboxylate derivative compounds as shown in the scheme 17. The published compounds are recrystallized from 3: 7 methanol-ethyl acetate mixtures. In another published article the Rajaraman *et al* [55] synthesised and reported some Novel (E)-(4-(2-(benzo[d]thiazol-2-yl)hydrazono)methyl-2,6-diphenylpiperidin-1-yl)(phenyl)methanone derivatives. The synthesised compounds was purified by column chromatography with ethyl acetate & hexane (1:4 ratio) mixture.



Scheme 17. Synthesis of some Ethyl 5-(1-methyl-1h-tetrazol-5-ylthio)-4-oxo-2,6-substituted diphenylpiperidine-3-carboxylate derivative.

The reported compounds are crystallised with ethanol. The reported crystal compounds exist in the normal chair confirmation as shown in the scheme 15.

Conclusion

This review shows that many of the piperidine-4-one and its derivatives synthesized in a wide range of synthetic techniques. Most of the synthesized compounds were recrystallized with distilled ethanol. Even though, some piperidine-4-one and its 2,6-disubstituted crystal structure were recrystallized with acetonitrile, methanol, benzene-petroleum, ethanol-ethyl acetate mixture, methanol-ethyl acetate mixture and dichloromethane/methanol (1:1, v/v). The evidence of the crystallographic data of the reported crystal structures shows that many crystal structures adopt a chair conformation. Whereas other conformation like a boat, twist boat, slightly distorted chair, and distorted boat also confirmed by crystallographic data.

References

[1] V. Perumal, M. Adiraj, P.S. Pandiyan, *Indian Drugs*, (2001), 38(3), 156-159.

[2] C. Ramalingan, Y.T. Park, S. Kabilan, *Eur J Med Chem*. (2006), 86, 1616.

[3] S. Balasubramanian, G. Aridoss, P. Parthiban, *Biol Pharm*, (2006), 58:125.

[4] S. Murugesan, S. Perumal, S. Selvaraj, *Chem Pharm Bull*, (2006), 54, 795.

[5] A. Manimekalai, J. Jayabarathi, L. Rufina, R. Mahendran, *Indian J Chem*, (2003), 428, 2074.

[6] C.R. Noller, V. Baliah, J Am Chem Soc, (1948), 376, 3853.

[7] P.S. Watson, B. Jiang, B. Scott, *Org. Lett*, (2000), 2, 3679-3681.

[8] D. Weintraub, P.J. Moberg, J.E. Duda, I.R. Katz, *Journal of Geriatric Psychiatry and Neurology*, (2003), 16(3), 178-183.

[9] Mannich, W. Korsche, *Arch Pharm*. (1912), 250, 647.

[10] C. Noller, V. Baliah, *J Am Chem Soc*, (1948) 70.

[11] V. Baliah, A. Ekambaram, T.S. Govindarajan, *Curr Sci*,1(954), 23, 264.

[12] V. Baliah, T.S. Govindarajan, *Sci*., (1954) 23, 91.

[13] V. Baliah, V. Gopalakrishnan, *J Indian Chem Soc*, (1954), 31, 250.

[14] V. Baliah, V. Gopalakrishnan, T.S. Govindarajan, *J Indian Chem Soc*, (1954), 31, 832.

[15] V. Baliah, A. Ekambaram, *J Indian Chem Soc*, (1955), 33, 274.

[16] P. Petrenko-Kritchenko, Lewin M. *Ber*. (1907), 40, 2882.

[17] P. Petrenko-Kritchenko, *Ber*. (1907), 42, 3683.

[18] P. Petrenko-Kritchenko, *Zh Russ Khim*, (1915) 47.

[19] P. Petrenko-Kritchenko, T.K.C.R. Chumanchenko, *Hebd Seances Acad Sci*, (1940), 27, 470.

[20] G. Aridoss, D. Gayathri, D. Velmurugan, M. S. Kim, Yeon Tae Jeong, *Acta Cryst*. (2009). E65, o2276–o2277

[21] K. Rajkumar, S. Sivakumar, R. Arulraj, M. Kaur, J.P. Jasinski, A. Manimekalai, A. Thiruvalluvar, *Acta Cryst E*, E74 (2018) 483–486.

[22] R. Arulraj, S. Sivakumar, Manpreet Kaur, A. Thiruvalluvar, J.P. Jasinski, *Acta Cryst E*, E73 (2017) 107–111.

[23] R. Arulraj, S. Sivakumar, A. Thiruvalluvar, Manpreet Kaur, J.P. Jasinski, *IUCrData*, (2016), 1, x161580.

[24] R. Arulraj, S. Sivakumar, K. Rajkumar, J.P. Jasinski, M. Kaur, A. Thiruvalluvar, *J. Chem. Crystallogr*., (2019), 50, 41-51.

[25] R. Arulraj, S. Sivakumar, S. Suresh, K. Anitha, *Spectrochim. Acta A*, (2020), 232, 118166.

[26] R. Arulraj, K. Sevgi, D. Necmi, S. Sivakumar, *J. Chem Crystallogr*, August 2020.

[27] K. Anitha, S. Sivakumar, R. Arulraj, K. Rajkumar, M. Kaur and J.P. Jasinski, *Acta Cryst E*., (2020), E76(5), 651–655.

[28] S. Murugesan, P.Subbu, S. Sangavanaicker, *Chem. Pharm. Bull*. 54(6), 795-801, (2006).

[29] A. Manimekalai, K. Selvaraju, T. Maruthavanan, *Ind. Jour. of Chemistry*, 46B, (2007), 160-169.

[30] V. Manjula, R. Venkateswaramoorthi, J. Dharmaraja, S. Selvanayagam, *IUCrData*, (2020), 5, x200526.

[31] P. Gayathri, A. Thiruvalluvar, A. Manimekalai, S. Sivakumar, R.J. Butcher, *Acta Cryst*. (2008), E64, o1973.

[32] N. Sampath, M.N. Ponnuswamy, *Mol. Cryst. Liq. Cryst*, (2006), 452, 93-101.

[33] B.N. Lakshminarayana, C.R. Gnanendra, T.N. Mahadeva Prasad, M.A. Sridhar, N. Naik, D. C. Gowda, J.S. Prasad, *J Chem Crystallogr*, (2010), 40, 686–690.

[34] R. Arulraj, S. Sivakumar, A. Thiruvalluvar, A. Manimekalai, *IUCrData*, (2016). 1, x160188.

[35] R. Arulraj, S. Sivakumar, A. Thiruvalluvar, A. Manimekalai, *IUCrData*, (2016). 1, x161982.

[36] R. Siddiqui, U. Iqbal, Z. S. Saify, S. Akhtera, S. Yousuf, *Acta Cryst*, (2018). E74, 931–934.

[37] S. Sivakumar, R. Arulraj, J.J.F. Xavier, H. Ramesh, K. Mageswari, A. Rajappa, *IJCPS*, 2014, 2(6), 911-918.

[38] C.R. Gnanendra, B.N. Lakshminarayana, G.B. Thippeswamy, M.A. Sridhar, N. Naik, J.S. Prasad, *Mol. Cryst. Liq. Cryst*, (2009), 515, 179–189.

[39] B. Raghuvarman, R. Sivakumar, V. Thanikachalam, S. Aravindhana, *Acta Cryst*. (2014), E70, 199–202.

[40] Yue Sun, Shu-Xia Wang, Gui-Ge Hou, Z. Kristallogr. *NCS* (2019), 234(5), 1047–1049.

[41] S. Amala, G. Rajarajan, E. Dhineshkumar, M. Arockia doss, V. Thanikachalam, S. Selvanayagam, B. Sridhar, *New J. Chem*, 2019.

[42] K. Selvaraju, A. Manimekalai, *Rasayan J. Chem*, (2017), 10(1), 25-31.

[43] T. Kuswardani, N. Herfindo, N. Frimayanti, R. Hendra, A. Zamri, *Molbank*, (2020), M1159.

[44] M. Thenmozhi, T. Kavitha, V. Mohanraj, S. Ponnuswamy, M.N. Ponnuswamy, *Acta Cryst*, (2009), E65, o2793.

[45] M. Thenmozhi, S. Ponnuswamy, V. Mohanraj, R. Vijayalakshmi, M.N. Ponnuswamy, *Acta Cryst*, (2009), E65, o11.

[46] D.S.M.S. ALkhafaji1, A.M. Fenjan1, A.T. Mohammad, *Journal of Al-Nahrain University*, (2018), 21(2), 64-72.

[47] P. Rajesh, M. Dinesh Kumar, R. Jamunarani, J. Manikandan, *Asian Journal of chemistry*, (2015), 27 (11), 3969-3974.

[48] C. R. Gnanendra, B. N. Lakshminarayana, G. B. Thippeswamy, M. A. Sridhar, Nagaraja Naik, J. Shashidhara Prasad, *Mol. Cryst. Liq. Cryst*, (2009), 515, 179–189.

[49] P. S. Anand, A. Sethukumar, C. Udhaya Kumar, B. Arul Prakasam, *Chemical Data Collections*, 2018, 15-16, 170-183.
[50] Y. Sun, S.X. Wang, G.G. Hou, *De Gruyter*, (2019). (DOI: https://doi.org/10.1515/ncrs-2019-0253).
[51] K. Sundaresan, M. Thangavel, K. Tharini, *Journal of Drug Delivery & Therapeutics*, (2019), 9(1), 233-236.
[52] K. Gokula Krishnan, R. Sivakumar, V. Thanikachalam, *J. Serb. Chem. Soc*, (2015), 80 (9), 1101–1111.
[53] T. Suresh, S. Sarveswari, N. Arul murugan, V. Vijayakumar, P. Iniyavan, A. Srikanth, Jerry P. Jasinski, *Journal of Molecular Structure*, (2015), 1099, 560-566.
[54] R. Srikanth, C.S. Venkatesan, P. Sugumar, A. Sivarajan, M.N. Ponnuswamy, *Der Pharma Chemica*, (2018), 10(7), 124-138.
[55] D. Rajaraman, G. Sundararajan, K. Krishnasamy, *International Letters of Chemistry, Physics and Astronomy*, (2015), 60, 35-46.

The reported compounds are crystallised with ethanol. The reported crystal compounds exist in the normal chair confirmation as shown in the scheme 15.