Indian Journal of Chemistry
Vol. 63, February 2024, pp. 159-165
DOI: 10.56042/ijc.v63i2.4442

Synthesis of fluorinated ferrocene derivatives for their thermal behavior and their *in silico* studies in designing of potential breast cancer inhibitors

Dinesh N Navale*[a], Prasanna B Ranade[a], Santosh W Zote[b], Dnyaneshwar K Kulal[c], Swapnil J Wagh[d] & Suresh T More[e]

[a] Department of Chemistry, Vivekanand Education Society's College of Arts, Science and Commerce, (Autonomous), Chembur, Mumbai 400 071, India

[b] Department of Chemistry, Sathaye Autonomous College of Arts, Science and Commerce, Vile Parle (East), Mumbai 400 057, India

[c] Department of Chemistry, Ramnarian Ruia Autonomous College, Matunga(East), Mumbai 400 019, India

[d] Department of Chemistry, Nanasaheb Y. N. Chavan Arts, Science and Commerce College Chalisgaon, Jalgaon 424 101, India

[e] Department of Chemistry, Arts Commerce and Science College, Kinhavali, Thane 421 403, India

E-mail: dineshnavale@gmail.com

Received 29 July 2023; accepted revised 24 January 2024

The docking studies of the different fluorinated ferrocene derivatives have been carried out against estrogen receptor enzymes. The docking results are very much comparable with standard drug tamoxifen. The designed fluorinated ferrocene derivatives show similarity in binding as tamoxifen exhibits estrogen receptor enzymes *in silico*. Docking studies reveal that designed fluorinated ferrocene derivatives have potential against breast cancer *in silico*. The ADME properties of some of the designed compounds are indicative of the drug likeness of compounds. All the designed fluorinated derivatives have been synthesized and have been evaluated for their thermal behavior.

Keywords: Docking, fluorinated ferrocene derivatives, ADME, Tamoxifen, Binding, DSC, Thermal behavior, Breast Cancer

Bio organometallic chemistry has gained great importance[1] in the last two decades due to the significance of organometallic compounds in the field of biology[2], chemical[3], pharmaceuticals[4] and materials chemistry[5]. Organometallic compounds give advantage to the organic compounds for additional properties of the metals including polarizability, color, magnetic, optical and electrical as compared to the normal organic compounds[6].

The popular family of organometallic compounds that comprises ferrocene illustrates exceptional thermal stability, aromaticity and a reactivity similar to that of other aromatic species, that allowed introduction of a huge number of substituents[7].

Large number of ferrocene derivatives are used in the field of electro analytical chemistry[8], hydrometallurgy[9], biology and medicine[10].

Ferrocene derivatives also exhibit antitumor properties. Ferrocene derivatives can also show antimalarial activity[1].

In addition to possessing a unique structure and exceptional redox properties, ferrocene is nontoxic[1]. An established drug's biological activity improves and its broad spectrum is generally enhanced, through the inclusion of a ferrocenyl moiety[1].

Low polarizability, high ionization potential and small Van der Waals radius of fluorine, very high electronegativity of fluorine[11] is also vital.

In biological substances[12], pharmaceuticals[13], agrochemicals[14], liquid crystals[15], dyes[16] and polymers[17] fluorine-containing functional groups constitute an invaluable component. Its introduction often remains a synthetic challenge.

The physico-chemical characteristics of an organic molecule are drastically changed once fluorine atoms become embedded in the structure of the molecule[18]. The aforementioned special qualities of fluorinated compounds have progressively strengthened the use of these compounds in a variety of industrial applications.

Fluorine functions, such as -RF, -F, $-CF_3$, $-OCF_3$ provide molecules with valuable drug-like physiological features that enhance receptor binding selectivity, improve lipophilicity and improve metabolic stability[19]. An important scientific endeavour is the practical synthesis of molecules that are composed of organofluorine.

In nature, amines and amides are abundant. They are essential components of proteins and enzymes, nucleic acids, and alkaloid drugs[20].

Docking

As stated by WHO reports every year millions of people are diagnosed with cancer[21]. Damage in the DNA results in mutation[22] which results in the improper functioning of cells, synthesis of proteins, enzymes which leads to cancer. Various cancers[23] such as prostate, pancreatic, breast and ovarian are caused due to genes like CHEK2 ATM and PALB2, BRCA1 and BRCA2.

Main reason for breast cancer in women are the mutations in BRCA1 and BRCA2 genes[24]. Estrogen and progesterone receptors play a vital role in breast cancer[7].

Estrogen and progesterone receptors are found in breast cancer[25]. Reducing the level of both of these receptors with the help of drugs will result in curing cancer patients. Cancer disease can be kept away by blocking these receptors[26] with the help of treatment of drugs. Tamoxifen[27], Toremifene[28] are the prominent drugs approved for the treatment of breast cancer. Thus blocking of estrogen receptors will be considered as an active site region against breast cancer *in silico*[29,30].

Several reports claim in the literature that ferrocene derivatives are docked for anticancer agents and can be used for anticancer[31-40]. Nowadays, docking[41-46] is an expeditious technique to identify the lead as well as target molecule against enzymes.

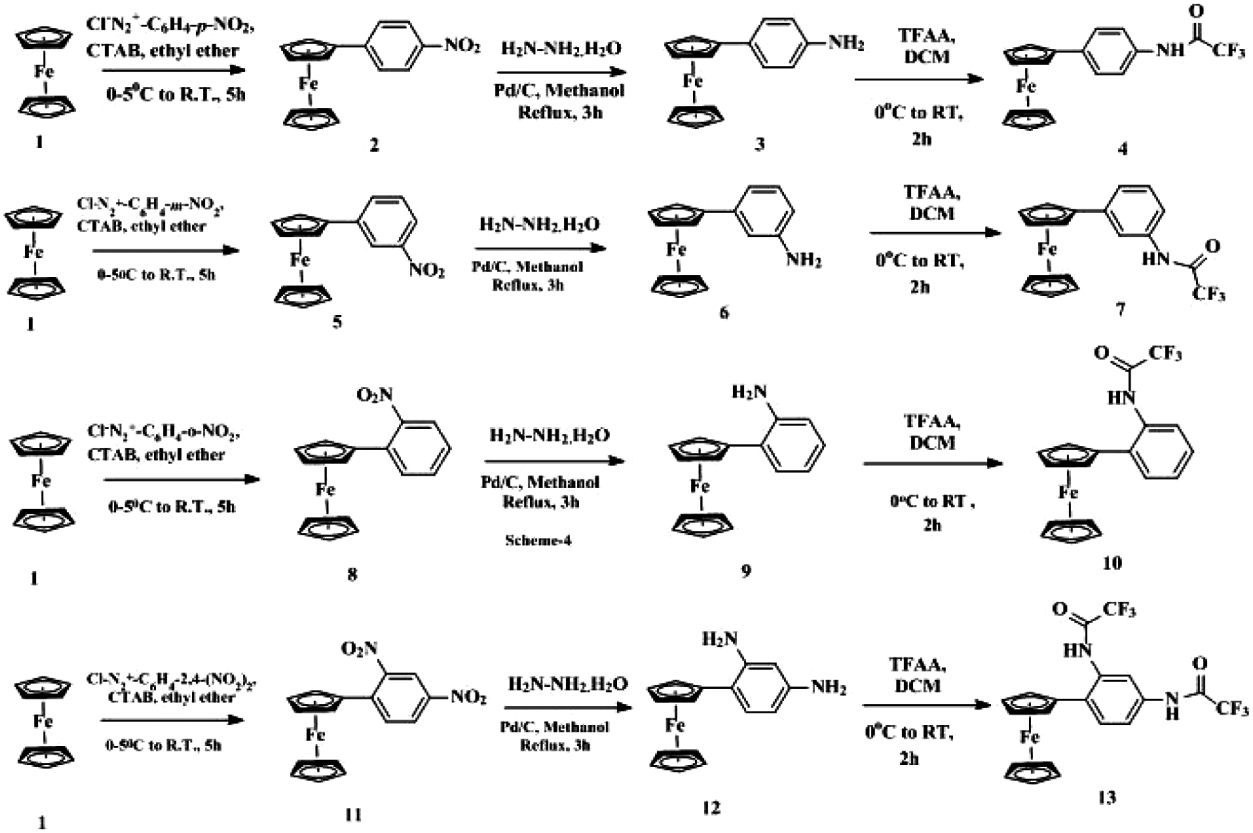
Hence we designed fluorinated ferrocene derivatives to treat breast cancer *in silico* using CB dock-a web based server. In present study, we are docking fluorinated ferrocene derivatives.

Due to the wide range of applications, it would be desirable to produce new derivatives based on fluorocarbon ferrocenes.

Taking into consideration the literature's comments, our interest is for new synthesis of new fluorinated ferrocene derivatives as potential candidates against estrogen receptors. We now report the docking and synthesis of novel fluorinated ferrocene derivatives as delineated in Scheme 1, Scheme 2 and Scheme 3.

Results and Discussion

Standard anticancer drug Tamoxifen is docked against estrogen receptors 29 using PDB ID 1A52. The dock score of tamoxifen is observed to be -9.1 which is comparable with fluorinated ferrocene derivatives. All the newly synthesized ferrocene drivatives have a dock



Scheme 1 — Synthesis of compounds **4**, **7**, **10** and **13**

score in range -7.3 to -9.1 The binding interaction of tamoxifen with amino acids Met343, Leu346, Thr347, Leu349, Ala350, Asp351, Glu353, Leu354, Trp383, Leu384, Leu387, Met388, Leu391, Arg394, Phe404, Met421, Ile424, Leu428, Gly521, Met522, His524, Leu525, Lys529 is observed. These amino acids are found in the binding pocket of estrogen receptors. All the newly synthesized fluorinated ferrocene drivatives bind commonly with amino acids in the active site of estrogen receptors which are similar to that of tamoxifen. This indicates fluorinated ferrocene derivatives have potential breast cancer characteristics *in silico*. (Supporting information contains docking images and ADME properties).

Docking studies

CB-Dock web server were used for the docking studies of Fluorinated ferrocene derivatives and estrogen receptor enzymes. Estrogen receptors were downloaded from www.rcsb.org PDB ID 1A52[47]. Docking studies of newly designed and synthesized compounds are shown in Table 1.

Ligands Preparation

ChemDraw software was used for the drawing of Fluorinated ferrocene derivatives. The structures drawn were saved in .sdf file format. SWISS ADME web based server was used for the evaluation and prediction of ADME properties[48]. ADME properties of newly designed and synthesized compounds are shown in Table 2.

Thermal Behaviour of Fluorinated ferrocene derivatives

With the aid of a differential scanning calorimetry DSC, all recently synthesized fluorinated ferrocene derivatives have also been assessed for their thermal behavior. Thermal studies confirm that all the synthesized compounds show remarkable thermal stability but none of them exhibited liquid crystalline behavior.

Experimental Section

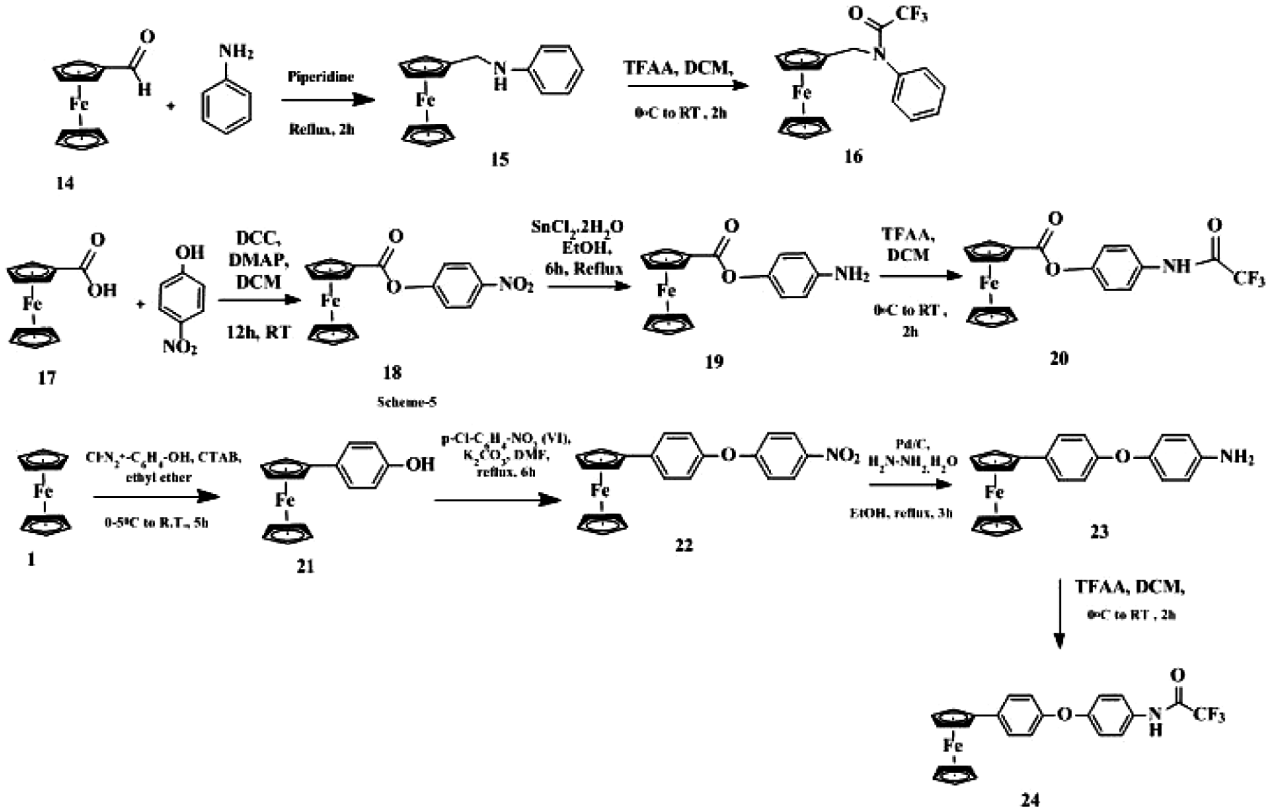
Preparation of 4- ferrocenylnitrobenzene, 2 (Ref. 49)

Synthesis of compound **2** was carried out by using the reported procedure[49].

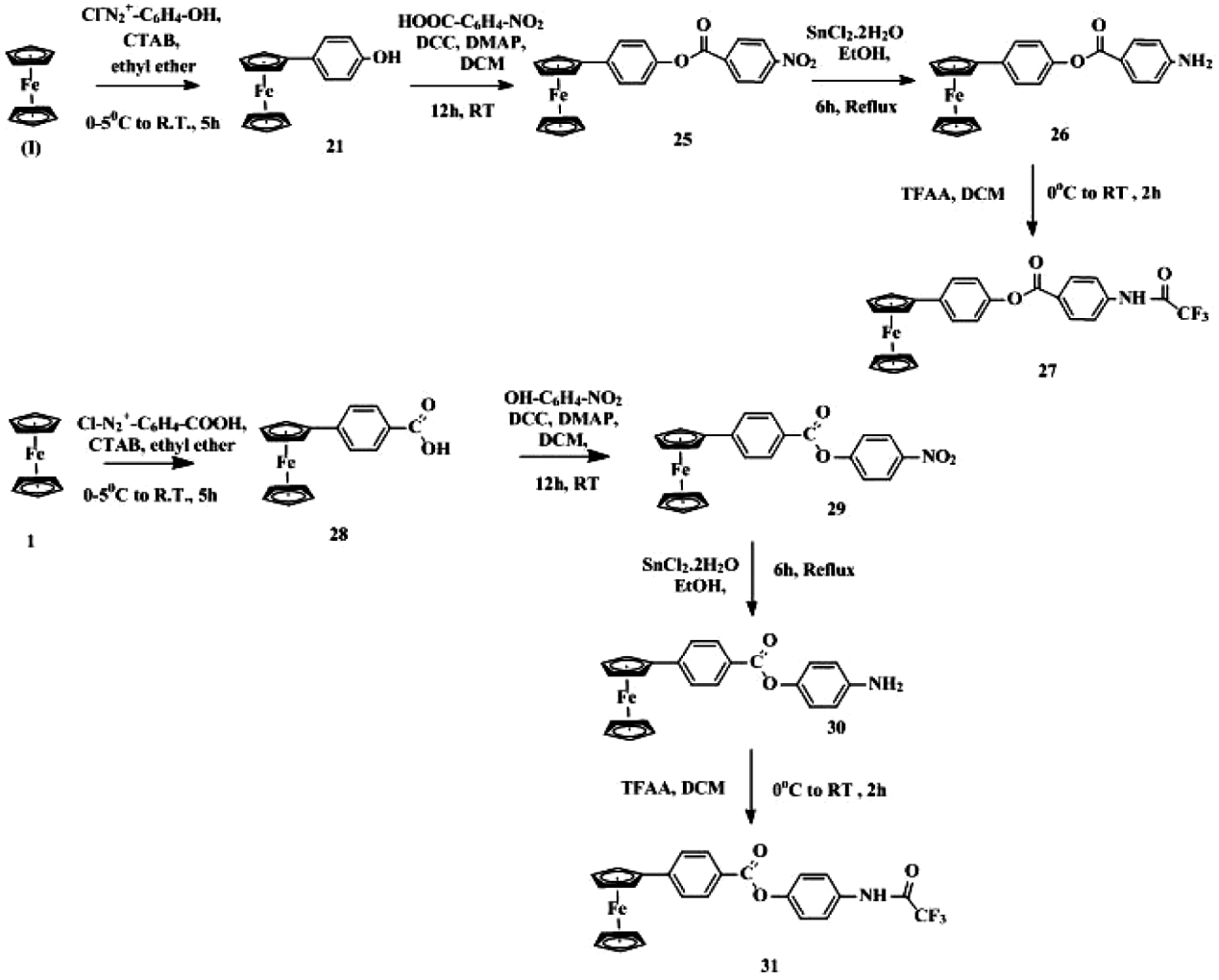
Preparation of 4- ferrocenylaniline, 3 (Ref. 50, 51)

Synthesis of compound **3** was carried out by using the reported procedure[50,51].

Synthesis of compounds (**5**, **6**, **8**, **9**, **11**, **12**) was carried out by using the same procedure as explained



Scheme 2 — Synthesis of compounds **16**, **20**, **24**



Scheme 3 — Synthesis of compounds **27** and **31**

Table 1 — Dock score of designed fluorinated ferrocene derivatives

S. No.	Compd	Dock Score
1	**4**	–7.3
2	**7**	–8.1
3	**10**	–8.5
4	**13**	–9.1
5	**16**	–8.0
6	**20**	–8.0
7	**24**	–8.6
8	**27**	–9.1
9	**31**	–9.1
10	Tamoxifen	–9.1

in synthesis of **2** and **3** [23,49,50]. Synthesis of compounds (**21**, **25**, **26**, **28**, **29**, **30**) was carried out by using the reported procedure[49]. Synthesis of compounds **18**, **19** was carried out by using the same procedure as explained for the synthesis of other derivatives[49]. Synthesis of compound **15** was carried out by using the reported procedure[49]. Synthesis of compounds **22** and **23** were carried out by using the reported procedure[51].

General procedure for the synthesis of compounds (4, 7, 10, 13, 16, 20, 24, 27, 31)

In a round bottom flask amines (0.0036 mol) was dissolved in 25 mL of dichloromethane. After cooling the reaction mixture at 0°C, trifluoroacetic anhydride (0.0036 mol) was slowly added, maintaining the temperature of the reaction below 0°C (entire addition takes place in 15 min.) After the complete addition the reaction was kept for stirring at RT for 2 h. After completion of the reaction the reaction mixture was concentrated under reduced pressure to afford the desired products **4**, **7**, **10**, **13**, **16**, **20**, **24**, **27**, **31**.

Physical and spectral data of synthesized compounds

4: Yield 95%. m.p.231-233°C. IR: 3290.61 (–CONH–), 3133.64 (C-H), 1698.24 (C=O of amide),

Table 2 — ADME properties of fluorinated ferrocene derivatives

S. No.	Compd	H-bond Acceptor	H-bond donor	Consensus Log P	ESOL Log S	GI Absorption	BBB	Log Kp	Lipinski
1	**4**	4	1	3.53	–5.53	High	Yes	–4.68	0
2	**7**	4	1	3.53	–5.53	High	Yes	–4.68	0
3	**10**	4	1	3.53	–5.53	High	Yes	–4.68	0
4	**13**	8	2	3.88	–6.17	Low	No	–5.14	0
5	**16**	4	0	3.62	–5.69	High	No	–4.61	0
6	**20**	6	1	3.17	–5.45	High	Yes	–5.18	0
7	**24**	5	1	4.57	–7.04	Low	No	–4.15	1
8	**27**	6	1	4.44	–7.06	Low	No	–4.4	1
9	**31**	6	1	4.44	–7.06	Low	No	–4.4	1
10	Tamoxifen	2	0	5.77	–6.59	Low	No	–3.5	1

1602.30 (C=C), 1497.52 (C=C of ferrocene), 1198.97 (C-F), 835.91 (of 1,4 disubstituted benzene), 514.09 cm^{-1} (Fe-cyclopentadiene stretching of ferrocene); ^{1}H NMR ($CDCl_3$): δ 8.149 (d, *J* = 6.9 Hz, 2H, Ar-H), 7.547 (d, *J* = 6.3 Hz, 2H, Ar-H), 4.803 (s, 2H, C_5H_4 of ferrocene), 4.529 (s, 2H, C_5H_4 of ferrocene), 4.112 (s, 5H, C_5H_5 of ferrocene), 2.310 (bs, 1H, -NH proton), MS: *m/z* 372.75.

7: Yield 95%. m.p. 139-141°C. IR: 3263.94 (–CONH–), 3094.54 (C-H), 1707.35 (C=O of amide), 1609.56(C=C), 1505.82 (C=C of ferrocene), 1195.50(C-F), 787.91 (of 1,3 disubstituted benzene), 506.02 cm^{-1} (Fe-cyclopentadiene stretching of ferrocene); ^{1}H NMR ($CDCl_3$): δ 7.945 (s, 1H, Ar-H), 7.651 (s, 1H, Ar-H), 7.323 (d, *J* = 9.6 Hz, 2H, Ar-H), 4.738 (s, 2H, C_5H_4 of ferrocene), 4.429 (s, 2H, C_5H_4 of ferrocene), 4.132 (s, 5H, C_5H_5 of ferrocene), 2.310 (bs, 1H, -NH proton), MS: *m/z* 372.78.

10: Yield 95%. m.p. 73-75°C. IR: 3338.01 (–CONH–), 3098.59 (C-H), 1723.92 (C=O of amide), 1605.82(C=C), 1492.08 (C=C of ferrocene), 1187.03(C-F), 732.37 (of 1,2 disubstituted benzene), 591.00 cm^{-1} (Fe-cyclopentadiene stretching of ferrocene); ^{1}H NMR ($CDCl_3$): δ 9.195 (bs, 1H, -NH proton), 8.185 (s, 1H, Ar-H), 7.548 (s,1H, Ar-H), 7.335(d, 2H, Ar-H), 4.522 (s, 2H, C_5H_4 of ferrocene), 4.496 (s, 2H, C_5H_4 of ferrocene), 4.252 (s, 5H, C_5H_5 of ferrocene), MS: *m/z* 372.74.

13: Yield 90%. m.p. 160-162°C. IR: 3263.94 (–CONH–), 3100.96 (C-H), 1731.86 and 1708.25 (C=O of amide), 1615.88(C=C), 1552.93 (C=C of ferrocene), 1180.14(C-F), 681.16, 793.92 and 830.48 (of 1,2 and 1,3 and 1,4 disubstituted benzene), 592.57 cm^{-1} (Fe-cyclopentadiene stretching of ferrocene); ^{1}H NMR (acetone): δ 10.434 (bs, 1H, -NH proton), 9.787 (bs, 1H, -NH proton), 8.202 (s, 1H, Ar-H), 7.601 (s, *J* = 7.5 Hz, 2H, Ar-H), 7.462(d, *J* = 7.8 Hz, 2H, Ar-H), 4.877 (s, 2H, C_5H_4 of ferrocene), 4.663 (s, 2H, C_5H_4 of ferrocene), 4.446 (s, 5H, C_5H_5 of ferrocene), MS: *m/z* 483.62.

16: Yield95%. m.p. 122-124°C. IR: 3355.55 (–CONH–), 3087.90 (C-H), 1688.41 (C=O of amide), 1595.72(C=C), 1495.98 (C=C of ferrocene), 1200.49(C-F), 480.84 cm^{-1} (Fe-cyclopentadiene stretching of ferrocene); ^{1}H NMR ($CDCl_3$): δ 7.382-6.997 (m, 5H, Ar-H), 4.667 (s, 2H, CH_2-N), 4.218 (s, 2H, C_5H_4 of ferrocene), 4.114 (s, 2H, C_5H_4 of ferrocene), 4.071(s, 5H, C_5H_5 of ferrocene), MS: *m/z* 386.70.

20: Yield93%. m.p. 156-158°C. IR: 3308.18 (–CONH–), 3106.78 (C-H), 1713.17 (C=O of ester), 1615.91 (C=O of amide), 1558.56(C=C), 1509.19 (C=C of ferrocene), 1198.50 cm^{-1} (C-F); ^{1}H NMR ($CDCl_3$): δ 7.535-7.506 (d, 2H, Ar-H), 7.117-7.088 (d, 2H, Ar-H), 2.189 (s, 1H, -NH), 4.967 (s, 2H, C_5H_4 of ferrocene), 4.547 (s, 2H, C_5H_4 of ferrocene), 4.321(s, 5H, C_5H_5 of ferrocene), MS: *m/z* 416.48.

24: Yield 95%), m.p. 158-160°C. IR: 3395.14 and 3348.19 (–CONH–), 3104.9 (C-H), 1719.12 (C=O), 1608.08 (C=C), 1452.77 (C=C of ferrocene), 1251.67 (C-F of), 851.25 (of 1, 4 disubstituted benzene), 503.40 cm^{-1} (Fe-cyclopentadiene stretching of ferrocene); ^{1}H NMR ($CDCl_3$): δ 8.048 (bs, 1H, NH-), 7.514 (d, *J* = 6.0 Hz, 2H, Ar-H), 7.367 (d, *J* = 6.9 Hz, 2H, Ar-H), 7.087 (d, 2H, Ar-H), 7.010 (d, *J* = 6.9 Hz, 2H, Ar-H), 5.161 (s, 2H, C_5H_4 of ferrocene), 4.842 (s, 2H, C_5H_4 of ferrocene), 4.467 (s, 5H, C_5H_5 of ferrocene), MS: *m/z* 464.54.

27: Yield 90%. m.p. 170-172°C. ^{1}H NMR ($CDCl_3$): δ 8.222 (d, *J* = 7.2 Hz, 2H, Ar-H), 8.095(d, *J* = 7.8 Hz, 2H, Ar-H), 7.969(d, *J* = 6.3 Hz, 2H, Ar-H), 7.741(d, *J* = 6.9 Hz, 2H, Ar-H), 5.233 (bs, 1H, NH),

4.858 (s, 2H, C_5H_4 of ferrocene), 4.538 (s, 5H, C_5H_5 of ferrocene), 4.426 (t, 2H, $C_5H_4$of ferrocene).

31: Yield 90%. m.p. < 210°C. ^{1}H NMR ($CDCl_3$): δ 8.121 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.591 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.035 (dd, *J* = 6.6 and 6.9 Hz, 2H, Ar-H), 6.748 (m, 2H, Ar-H and NH proton), 4.760 (t, 2H, C_5H_4 of ferrocene), 4.431 (t, 2H, C_5H_4 of ferrocene), 4.426 (s, 5H, C_5H_5 of ferrocene).

Conclusion

In conclusion, readily available and cheap chemicals were used to synthesize new fluorine substitutes based on ferrocene derivatives at good yields.

The dock score of tamoxifen is comparable with newly designed and synthesized fluorinated ferrocene derivatives. From docking studies it can be concluded that the binding of tamoxifen and fluorinated ferrocene derivatives with amino acid residues at the active site of the bonding pocket of estrogen receptors are the same. This indicates fluorinated ferrocene derivatives have potential breast cancer characteristics *in silico*. It can be concluded that fluorinated ferrocene analogs have potential anti-cancer activities *in silico*.

Blind docking helps in identifying potential target molecules for their activity against breast cancer. CB dock program helps in predicting the potential anticancer agents from dock score in less time.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

References

1 Mohammad F R, Fouda M M, Abd-Elzaher, Rafeek A A & Ammar A L, *Appl Organomet Chem*, 21 (2007) 613.
2 Patra M & Gasser G, *Chem Biochem*. 13 (2012) 1232.
3 Parshall G W, Nugent W A, Chan D M-T & Tam W, *Pure Appl. Chem*, 57 (1985) 1809.
4 Gasser G, Ott I & Metzler-Nolte N, *J Med Chem*, 54 (2011) 3.
5 Schwartz J & Bernasek S L, *Catalysis Today*, 66 (2001) 3.
6 Espinet P, Esteruelas M A, Oro L A, Serrano J L & Sola E, *Coord Chem Rev*, 117 (1992) 215.
7 Togni A & Hayashi T (Eds.), Ferrocenes: Homogeneous Catalysts, Organic Synthesis and Material Science, (VCH, Verlagsgesellschaft, Weinheim), 1995. (https://doi.org/10.1002/recl.19961151012).
8 Skeika T, Zuconelli C R, Fujiwara S T & Pessoa C A, *Sensors*, 11 (2011) 1361.
9 Beer P D, Szemes F, Balzani V, Sala C M, Drew M G B, Dent S W & Maestri M, *J Am Chem Soc*, 119 (1997) 11864.
10 Biot C, Glorian G, Maciejewski L A, Brocard J S, Domarle O, Blampain G, Millet P, Georges A J, Abessolo H, Dive D & Lebibi J, *J Med Chem*, 40 (1997) 3715.
11 Huchet Q A, Kuhn B, Wagner B, Fischer H, Kansy M, Zimmerli D, Carreira EM & Müller K, *J Fluorine Chem,* 152 (2013) 119.
12 Eric P G, Kyle J E, Matthew D H, David J D & Nicholas A M, *J Med Chem*, 58 (2015) 8315.
13 Munenori I, Yuji S & Norio S, *ACS Omega,* 5 (2020) 10633.
14 Qiang W, Hongjian S & Qingmin W, *Chinese Chem Lett*, 33 (2022) 626.
15 Peer K, *J Fluorine Chem*, 177 (2015) 29.
16 Yaguporskii LM, Il'chenko AY & Gandel'sman L Z, *Russian Chem Rev*, 52 (1983) 993.
17 Vanessa F C, Daniela M C, Clarisse R, Margarida M F & Senentxu L M, *Polymers*, 10 (2018) 161.
18 Poonam S & Andrew D W, *J Enzyme Inhib Med Chem*, 22 (2007) 527.
19 Bohm H, Banner D, Bendels S, Kansy M, Kuhn B, Muller K, Obst-Sander U & Stahl M. *Chem Biochem,* 5 (2004) 637.
20 Shikha K, Angelica V C, Amit K T & Paul C, Trippier, *J Med Chem,* 63 (2020) 12290.
21 WHO report on cancer: setting priorities, investing wisely, and providing care for all/ ISBN 978-92-4-000129-9 (electronic version) ISBN 978-92-4-000130-5 (print version).
22 Turgeon M-O, Perry N J S & Poulogiannis G, *Front Oncol*, 8 (2018) 1.
23 Russo A, Incorvaia L, Capoluongo E, Tagliaferri P, Gori S, Cortesi L, Genuardi M, Turchetti D, Giorgi U D, Maio M D, Barberis M, Dessena M, Re M D, Lapini A, Luchini C, Jereczek-Fossa B A, Sapino A & Cinieri S, *ESMO Open*, 7 (2022) 1.
24 Ghunaim H, Laenen A, Keyzer F.De, Soens J, .Keupers M, Postema S, Neven P & Van Ongeval C, *Eur J Radiology*, 146 (2022) 110074.
25 Munteanu A, Patrascu A & Ferariu D, *Rev Chim*, 68 (2017) 2570.
26 Kadamb R, Leibovitch B A, Farias E F, Dahiya N, Suryawanshi H, Bansal N & Waxman S, *Translational Oncology*, 16 (2022) 101320.
27 Kleijburg A, Braal C L, Westenberg J D, Jager A, Koolen S L W, Mathijssen R H J, Groot C A U-D, Wetzelaer P & Penton H, *Biomed Pharmacother*, 158 (2023) 114158.
28 Zhou Y, Fan Y, Ma L & Nowen J, *World Neurosurgery*, 149 (2021) 436.
29 Shanle E K & Xu W, *Adv Drug Deliv Rev*, 30 (2010) 1265.
30 Rocha-Roa C, Cortes E, Cuesta S Á, Mora J R, Paz J L, Flores-Sumoza M &. Marquez EA, *Comp Bio Med*, 152 (2023) 106403.
31 José A, Carmona N, Alberto S & Arnold L, Rheingold & Meléndez E, *Dalton Trans*, 48 (2019) 5952.
32 Sijongesonke P & Blessing A A, *Molecules,* 24 (2019) 3604.
33 Jun M, Xin X, Shanshan X, Yuehua, Yuting W, Qian Z, Hongping Z, Wei H & Gu H, *Chinese Chem Lett*, 32 (2021) 1897.
34 Bharvi S, Liang G, Ruvesh P P, Nosipho C, Paul A, Parvesh S, Mandeep K & Vipan K, *New J Chem*, 44 (2020) 11137.
35 Khalaf M M, El-Lateef H M A, Alhadhrami A, Sayed F N, Mohamed G G, Gouda M, Shaaban S & Abu-Dief A M, *Materials (Basel)*, 20 (2022) 3678.

36 Gormen M, Pigeon P, Wang Y, Vessieres A, Top S, Martial F, Gros C, McGlinchey M A & Jaouen G, *Eur J Inorg Chem*, 2017 (2017) 454.
37 Walaa H M, Nessma F M & Gehad G M, *J Coord Chem*, 70 (2017) 3552.
38 Meral G, Damian P, Pascal P, Elizabeth A H, Marie-Aude P, Siden T, Anne V & Gérard J, *Tetrahedron Lett,* 51 (2010) 118.
39 Rana M, Perotti A, Bisset L M, Smith J D, Lamden E, Khan Z, Ismail M K, Ellis K, Armstrong K A, Hodder S L, Bertoli C, Meneguello L, Bruin R A M D, Morris J R, Romero-Canelon I, Tucker J H R & Hodges N J, *Metallomics,* 14 (2022) (https://doi.org/10.1093/mtomcs/mfac041).
40 Mohamed M H, Muhammad K, Marwa A M l, Johan V E, Radwan A, Hamada S A & Ahmed A A K, *J Biomol Structure Dynamics*, 41 (2023) 5199.
41 Danel T, Łęski J, Podlewska S & Podolak I T, *Drug Disc Today*, 28 (2023**)** 103439.
42 Ranade P B, Navale D N, Zote S W, Kulal, D K & Wagh S J, *Indian J Biochem Biophy,* 60 (2023) 55.
43 Ranade P B, Navale D N, Ubaidullah A A, Dheeraj M N, Jajoriya C C & Mane P P, *Heterocyc Lett,* 13 (2023) 297.
44 Manisha C, Dolly S, Manas D & Karabi D, *Indian J Biochem Biophys*, 59 (2022) 38.
45 Jenny J & Kumar P B, *Indian J Biochem Biophys*, 58 (2021) 244.
46 Ganeshpurkar A & Saluja A, *Indian J Biochem Biophys*, 56 (2019) 28.
47 Yugandhar P, Kumar K K, Neeraja P & Savithramma N, *J Intercult Ethnopharm,* 12 (2017) 296.
48 Bakchi B, Krishna A D, Sreecharan E, Ganesh V B J, Niharika M, Maharshi S, Puttagunta S B, Sigalapalli D K, Bhandare R R & Shaik A B, *J Mole Structure*, 1259 (2022) 132712.
49 Carlescu I, Scutaru A M, Apreutesei D, Alupei V & Scutaru D, *Appl Organomet Chem*, 21 (2007) 661.
50 Akhter H N Z, Sumaira Y H M, Mirza B & Rifat A, J *Organomet Chem*, 694 (2009) 2198.
51 Navale D N, Zote S W & Ramana M M V, *J Applicable Chem*, 4 (2015) 1180.